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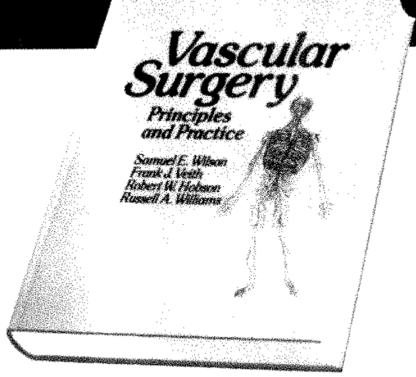

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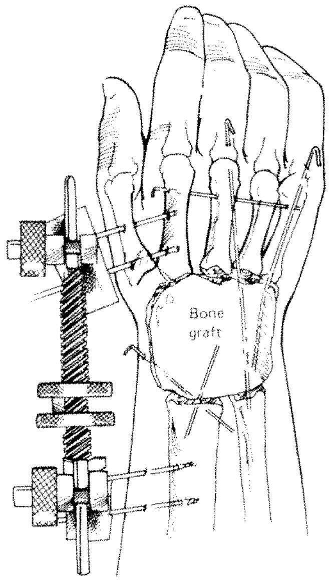

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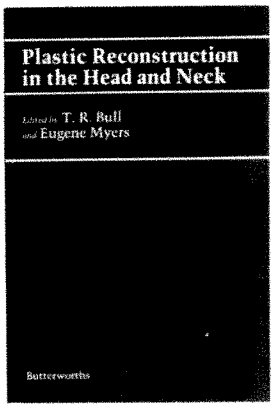
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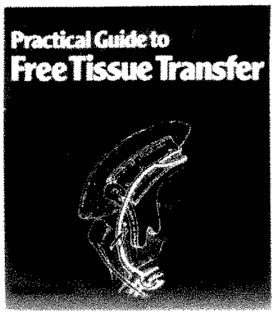

Free tissue transfer is a most valuable and versatile technique. A single chapter is devoted to each donor area and the authors describe in detail the vascular basis, surgical technique, donor defect, uses, and advantages and disadvantages of each procedure. Two-colour line drawings are used to clarify the anatomical and technical points of preparation of tissues for free tissue transfer. This book simplifies the technical aspects and dispels the mystique surrounding the technique. It should do much to ensure its widest acceptance by plastic and reconstructive surgeons.

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Br. J. Surg. 1987, Vol. 74, February, 79–80

Treatment of pancreatic carcinoma: the surgeon's dilemma

The vexed issue of surgery for pancreatic cancer has been the subject of a number of comprehensive recent reviews[1,7,8,10]. My remarks on the subject are going to be personal and are based on our experience with 560 patients referred to our surgical clinic in Mannheim with a diagnosis of pancreatic carcinoma. We have dealt with a further 102 patients with 'periampullary cancer' but in our experience these patients have a higher resectability rate (75 per cent) and 5 year survival rate (42 per cent) and I will not consider this condition further.

When it comes to the surgical treatment of pancreatic cancer, surgeons today are divided into three camps: the nihilists, the activists and the realists. The nihilists advocate some form of palliative procedure even for potentially operable lesions[3,9]. They argue that high operative mortality and poor long-term survival rates make any radical resection valueless. They further claim that after palliative bypass more patients live longer and more comfortably than after some form of pancreatectomy. However, there has been no controlled trial to substantiate this hypothesis and such a trial would be unlikely to pass the local ethics committee.

In our experience, the very opposite appears to be true: of 276 patients treated by some form of palliative bypass the operative mortality was 12 per cent and the median survival time amounted to 5·5 months. It should be noted that even non-operative endoscopic insertion of a transpapillary stent carries a 16 per cent 30 day mortality in experienced hands[2]. At the same time 91 of our patients with carcinoma of the pancreas were treated by radical resection with a mortality of 3·3 per cent and a median survival of 15·5 months. Of course these two groups of patients are in no way comparable; if anything, the bias is weighted heavily against the 'palliative' group, the inoperable ones. But it is not so much the length of survival but the quality of that survival, difficult to measure I know, that in our experience weights the scales in favour of resection. Always provided, of course, that enough patients survive resection to reap the benefits at least of palliation.

The activists recommend an extensive so-called regional pancreatectomy whenever possible[4]. The procedure includes subtotal or total pancreatectomy with *en bloc* regional lymph node dissection, as well as resection and reconstruction of large retropancreatic vessels (usually the portal vein). In essence, this is the old surgical dream of curing cancer by extending radicality. It has not worked out convincingly for the stomach, the breast or bronchus, so why should it work with pancreatic cancer? Fortner is to be commended for pursuing this philosophy to its logical conclusion[4,5] but his results have not encouraged many others to follow him. He reports on 61 regional pancreatectomies with an overall operative mortality of 23 per cent. Only 35 of this group of patients actually had carcinoma of the pancreas. Here the operative mortality was 26 per cent while 28 per cent died of recurrent cancer and 26 per cent of other causes. This left 7 of 35 patients (20 per cent) still alive at the time of writing, these patients only having survived that formidable operation for between 3 and 18 months.

That is why I cannot recommend routine regional pancreatectomy; there are situations however where it may become necessary. We were faced with this dilemma 16 times when late in the course of a Whipple procedure the portal vein was found to be infiltrated by tumour from behind. The pre-operative angioportogram had failed to show this infiltration in these particular cases. Since the tumour seemed to be otherwise operable and a 'point of no return' had been reached, we resected segments of the portal and/or superior mesenteric veins *en bloc* with the specimen. Reconstruction by simple suture, end-to-end anastomosis or mesentericocaval shunt was possible without operative mortality. The median survival time of these 16 patients amounted to only 12 months. But one of them is still alive 8 years after total pancreatectomy with portal vein resection for a T_3N_1 tumour.

That leaves the realists – and who among us does not see himself in this camp? The realists offer radical resection – total, partial or so-called conservative pancreaticoduodenectomy – to all patients with tumours that appear operable. At first sight total pancreatectomy seems to be the better cancer operation since it is in essence

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more 'radical', eradicating any multifocal disease and permitting wider lymph node clearance. But, as with regional pancreatectomy, this has not paid off so far in terms of longer survival[7]. Similarly, total pancreatectomy would seem to be the safer operation, avoiding as it does that potentially lethal pancreaticojejunal anastomosis. But again morbidity and mortality are higher for total than for partial pancreatectomy in most series, including our own where the overall mortality for total pancreatectomy is 3 out of 49 (6 per cent) as against 6 out of 217 for the Whipple operation (2·7 per cent). So it is our policy to do a Whipple procedure for all operable periampullary cancers and those of the head of the pancreas. Total pancreatectomy is reserved for patients whose tumours approach the line of a potential Whipple resection, whose pancreatic remnant is so friable that anastomotic complications are likely to ensue, and possibly for some patients who already are insulin dependent diabetics.

With more patients surviving pancreatic resection for cancer, it is only to be expected that long-term survival will also improve. We believe that we are beginning to see this effect when we look at 37 patients who had resection for pancreatic cancer before July 1981 (i.e. more than 5 years ago). Nine of these patients achieved 5 year survival. Of course it is inappropriate to express this statistically as a 24 per cent 5 year survival rate; particularly as four of these nine patients have since died, three of them from proven recurrent pancreatic cancer. So we must admit that surgery alone cannot solve the problem of pancreatic cancer. But until earlier diagnosis and really new adjuvant modalities are found, it is the only effective treatment we have. While the results of this surgery are not good, they are not bad enough to justify surgical nihilism.

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1. Carter DC. Surgery for pancreatic cancer. *Br Med J* 1980; **1**: 744–6.
2. Cotton PB. Endoscopic methods for relief of malignant obstructive jaundice. *World J Surg* 1984; **8**: 854–61.
3. Crile G Jr. The advantages of bypass operations over radical pancreatoduodenectomy in the treatment of pancreatic carcinoma. *Surg Gynecol Obstet* 1970; **130**: 1049–53.
4. Fortner JG. Regional resection of cancer of the pancreas: a new surgical approach. *Surgery* 1973; **73**: 307–20.
5. Fortner JG. Regional pancreatectomy for cancer of the pancreas, ampulla, and other related sites. *Ann Surg* 1984; **199**: 418–25.
6. Gudjonsson B, Livstone EM, Spiro HM. Cancer of the pancreas. Diagnostic accuracy and survival statistics. *Am Cancer* 1978; **42**: 2494–506.
7. van Heerden JA. Pancreatic resection for carcinoma of the pancreas: Whipple versus total pancreatectomy – An institutional perspective. *World J Surg* 1984; **8**: 880–8.
8. Longmire WP. The vicissitudes of pancreatic surgery. *Am J Surg* 1984; **147**: 17–24.
9. Shapiro TM. Adenocarcinoma of the pancreas: A statistical analysis of biliary bypass vs Whipple resection in good risk patients. *Ann Surg* 1975; **182**: 715–21.
10. Smith R. The choice between conservative and radical surgery in cancer in the upper abdomen. *Arch Surg* 1986; **121**: 391–4.

Br. J. Surg. 1987, Vol. 74, February, 81–82

Perforated duodenal ulcer

Simple closure of a perforated ulcer with an omental patch is quick and safe: mortality is usually related to the condition of the patient and the adequacy of resuscitation rather than to the procedure itself. Long-term follow-up of patients so treated shows that as many as 70 per cent experience further ulcer symptoms or complications and 20–40 per cent later require a definitive acid-reducing operation; one recent study has found that as many as 58 per cent come to further surgery[1]. It has been recognized for many years that patients with a long dyspeptic history are most likely to have ulcer recurrence after perforation[2]. It has become common practice to divide patients into acute and chronic ulcer categories depending on whether their dyspeptic history exceeds 3 months. The argument in favour of definitive surgery at the time of perforation for patients with chronic ulcer is supported by recent retrospective[3] and prospective studies[4]. Although a vagotomy operation prolongs the operative time, there is no evidence that it increases mortality, provided that patients are not shocked on admission, do not have severe concurrent disease and have been fully resuscitated[5]. It is commonly stated that a definitive operation must only be performed within 12 hours of perforation, but this is an arbitrary deadline and good pre-operative preparation of the patient is far more important than adhering rigidly to such a time limit.

It is important to look at the other side of the argument. There are several reasons why a policy of definitive surgery may not be universally acceptable. There is overlap between the acute and chronic ulcer groups and the 3 month rule is only arbitrary. Prospective follow-up has shown that, in the 2 years after perforation, 25–30 per cent of the 'acute' group and only 50 per cent of the 'chronic' group have proven ulcer recurrence[6]. One reason for this is the failure to consider operative findings in categorizing the patients; we have all operated on totally asymptomatic patients with a grossly scarred duodenum and at least 20 per cent of patients with duodenal ulcer may have asymptomatic disease. A further and important source of error is the assumption that an accurate ulcer history can always be obtained from a patient with peritonitis, either before or after opiate analgesia. As many as 50 per cent of patients may be wrongly classified by this type of pre-operative assessment[7]. Any definitive ulcer operation is irreversible and we have, therefore, to be sure that the patient does require this form of treatment. A definitive operation on all patients with a chronic ulcer history will result in about 30 per cent having a totally unnecessary procedure. A further 20–30 per cent would have had further ulcer symptoms that, even before H_2 blockers, could have been controlled by medical means. Therefore, 50–60 per cent of patients who may not have needed an operation are exposed to the potential long term side-effects of ulcer surgery. Whatever your philosophy towards the surgery of this condition, this does seem hard to justfiy.

The simple closure *versus* definitive surgery argument is very much one of the 1960s and 1970s and in the 1980s we must now decide what role, if any, H_2 blockers have in patients with perforated duodenal ulcer. At present we cannot answer this question because we do not have enough prospective data. Quite simply many surgeons are not applying the same proven principles of treatment and assessment of ulcer healing to post-perforation patients which physicians are using in the management of uncomplicated duodenal ulcer disease[8]. After simple closure most would give a minimum of 2 months of full dose cimetidine or ranitidine, but do perforated ulcers heal on such treatment? Only about 90 per cent of uncomplicated duodenal ulcers heal on such a regimen and, if perforation is a marker of a more severe ulcer diathesis, healing rates may be lower. We must also endoscope these patients to assess healing; it is not good enough to assume healing.

Once the ulcer is healed should we give long term maintenance treatment or stop treatment and 'wait and see'? Only about a third of those with acute ulcer perforation will have ulcer recurrence and it would seem logical to stop treatment after healing and identify this sub-group when they get recurrence. We know from many studies before the introduction of H_2 blockers that 70–80 per cent of the chronic ulcer group will require further treatment so it seems reasonable to give them long-term maintenance treatment. It cannot be emphasized too strongly that H_2 blockers do not cure the ulcer diathesis, they reduce acid secretion and allow ulcers to heal and remain healed. Our present knowledge of these drugs is that they do not alter the natural history of duodenal ulcer disease and they must be given for prolonged periods. To give a 3 or 6 month course to a patient with duodenal ulcer disease and then simply stop is just

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delaying the inevitable ulcer recurrence. Patients taking maintenance treatment should be followed for at least 6 months after healing as those who relapse on the reduced dosage, together with those who fail to heal on standard doses, need more thorough investigation and some will require surgery according to the same criteria as used in uncomplicated ulcer disease.

One further consequence of H_2 blockers is that surgeons-in-training are probably not performing enough ulcer surgery to be able to regard themselves as truly proficient. Those patients who require definitive surgery may be better served by having this performed later by an experienced surgeon with a proven track record in ulcer surgery.

In this issue of the journal Simpson *et al.* are getting to grips with the real question that we need to be asking in the 1980s – 'what is the role of H_2 blockers in perforated duodenal ulcer?' Only large prospective studies with endoscopic assessment and longer follow-up are going to answer this question, but it is time to resolve the controversy. For the moment we believe that the 'man on the spot' should content himself with adequate resuscitation of the patient and simple closure of the perforation. Then full doses of H_2 blockers should be commenced until endoscopic confirmation of healing is evident. Prolonged treatment may be needed in those patients with chronic ulceration. We suggest that the only patients who should be considered for emergency definitive surgery are those who perforate while taking H_2 blockers or who have had a previous ulcer complication[9].

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1. Ceneviva R, De Castro e Silva O, Castelfranchi PL, Modena JLP, Santos RF. Simple suture with or without proximal gastric vagotomy for perforated duodenal ulcer. *Br J Surg* 1986; **73**: 427–30.
2. Illingworth CFW, Scott LDW, Jamieson RA. Progress after perforated peptic ulcer. *Br Med J* 1946; **i**: 787–90.
3. Gillen P, Ryan W, Peel ALG, Devlin HB. Duodenal ulcer perforation: The effect of H_2 antagonists? *Ann R Coll Surg Engl* 1986; **68**: 240–22.
4. Boey J, Lee NW, Koo J, Lan PHM, Wong J, Ong GB. Immediate definitive surgery for perforated duodenal ulcers. *Ann Surg* 1982; **196**: 338–42.
5. Boey J, Wong J, Ong GB. A prospective study of operative risk factors in perforated duodenal ulcers. *Ann Surg* 1982; **195**: 265–9.
6. Boey J, Lee NW, Wong J, Ong GB. Perforation in acute duodenal ulcers. *Surg Gynecol Obstet* 1982; **155**: 193–7.
7. Baekgaard N, Lawaetz O, Ejby Poulson P. Simple closure of definitive surgery for perforated duodenal ulcer. *Scand J Gastroenterol* 1979; **14**: 17–20.
8. Bardhan KD. Long-term management of duodenal ulcer – a physician's view. In: Baron JH, ed. *Cimetidine in the 1980s*. London: Churchill Livingstone, 1981.
9. Sherlock DJ, Holl-Allen RTJ. Duodenal ulcer perforation whilst on cimetidine therapy. *Br J Surg* 1984; **71**: 586–8.

Review

Br. J. Surg. 1987, Vol. 74, February, 83-88

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Place of surgery in the management of amyloid disease

Amyloidosis is the generic term[1,2] for a group of uncommon disorders characterized by the extracellular deposition of abnormal protein material[3-5]. Despite their similarity under light and electron microscopy[1,5-7], striking differences have been demonstrated in the major components of several types of amyloid deposit[1]. Amyloid may be deposited at local sites or systemically and can affect any tissue[8,9]. Amyloid deposits tend to persist[10] producing functional impairment of affected tissues and, if sufficiently large, cause symptoms by obstruction or pressure on nearby structures[8,9]. Treatment is evolving but is generally unsatisfactory[3,6,11,12], and in its systemic form amyloidosis is ultimately fatal[11]. Supportive care is therefore, an important facet of treatment. Approximately 10 per cent of patients will initially present to the surgeon[12]. Excision of localized deposits may be curative, and in systemic amyloidosis surgery may improve survival.

Classification

Amyloid is classified on the basis of the predominant fibril type, and the underlying clinicopathological process[2,5,8] and one classification is shown in *Table 1*. In primary amyloidosis there is no recognized underlying disease[9], although in approximately 25 per cent of patients there is an associated plasma cell dyscrasia (myeloma associated amyloidosis)[7,12]. The fibrils are made up of proteins of the AL type (amyloid light chain protein). These are thought to derive from immunoglobulin light chains, or subunits of light chains and originate from plasma cells[1]. Many patients with primary amyloidosis, particularly those with myeloma associated disease, show Bence-Jones proteins in the serum and urine; proteolytic digestion of these proteins *in vitro* has produced fibrils similar to those of amyloid[1].

Secondary amyloidosis is found associated with chronic infections and inflammations, and with several types of neoplasia[13]. The fibrils consist of a protein that is unrelated to the immunoglobulins[14], and is known as amyloid A protein (AA fibril type). This protein is thought to derive from a cleavage product of serum amyloid A related protein (SAA)[1,2]. The levels of this protein rise with age and also increase in chronic inflammatory disorders[1].

A number of genetically determined amyloid syndromes (heredo-familial amyloidoses) have been described. All are uncommon and present with specific patterns of organ involvement and clinical manifestations[8,9,16,17]. The mode of inheritance is usually autosomal dominant, although recessive transmission has been reported with the amyloidosis associated with familial mediterranean fever[9]. Localized amyloidoses are usually associated with proteins of the AL type[8], but in many of the clinical forms the fibril types have not been fully characterized.

Table 1 *Classification of amyloidosis*

Clinical condition	Tissue distribution	Amyloid fibril type
Primary amyloidosis		
Primary (no preceding or coexisting disease)	Systemic	AL
Immunocyte dyscrasia-related	Systemic	AL
Myeloma		
Walderstrom's macroglobulinaemia		
Monoclonal gammopathy		
Plasmacytomas	Organ limited	AL
Secondary amyloidosis		
Chronic inflammation	Systemic	AA
Rheumatoid arthritis		
Ankylosing spondylitis		
Crohn's disease		
Chronic infections		
Osteomyelitis		
Paraplegia		
Tuberculosis		
Leprosy		
Bronchiectasis		
Burns		
Neoplasia		
Hodgkin's disease		
Hypernephroma		
Bronchogenic carcinoma		
Malignant melanoma		
Heredofamilial amyloidosis		
Neuropathic forms	Systemic with specific organ predilection	AF/?
Non-neuropathic forms	Systemic with specific organ predilection or purely localized	AA/?
Endocrine		
Islets of Langerhans	Localized	?
Insulinoma		?
Medullary carcinoma (thyroid)		AE_t
Miscellaneous		
Cerebral plaques	Localized	?
Cutaneous deposits		?
Cardiac involvement		ASc_1/?

The composition of amyloid fibrils in several clinical forms of amyloid has been determined by amino-acid sequencing. AL fibrils are composed of intact and/or fragments of immunoglobulin light chains. AA fibrils are composed of a unique protein with 76 amino acids. AF fibrils are composed of prealbumin and ASc_1 fibrils are related to prealbumin. AE_t fibrils are related to calcitonin precursor[2,5,8]

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Incidence

Autopsy studies have shown evidence of systemic amyloidosis in 0·26–1·09 per cent of cases, and microdeposits of amyloid have been reported in 18 per cent when consecutive autopsy cases were studied in great detail[18]. Senile deposits appear to be a normal concomitant of aging and are found in almost all patients over the age of 65 years, particularly in the brain, heart and pancreas[5,8].

Symptomatic amyloid is uncommon: Browning *et al.*[12] reported only 131 cases of histologically proven amyloidosis in a regional amyloid clinic over a 10 year period. Of these 124 were systemic in type and 7 were localized. Reports from America have suggested that primary amyloidosis has become the commonest form of amyloidosis in the Western world in recent years[1]. In Britain, however, secondary amyloidosis has been found to be more common accounting for 58–65 per cent of cases of amyloidosis[12,19].

Structure and pathogenesis

Amyloid is an extracellular, homogeneous, eosinophilic material (*Figure 1*) which stains with Congo Red and displays an apple green birefringence[5]. By electron microscopy amyloid has been shown to consist largely of fine non-branching fibrils which are made up of smaller filaments consisting of polypeptide chains lying in anti-parallel β pleated sheets. A further 5–10 per cent of amyloid is derived from plasma (protein AP)[2] and may act as a focus for the deposition of amyloid fibrils[10].

Amyloid fibrils cause little inflammatory response in the tissues and do not seem to stimulate phagocytic cells[10]. In addition the fibrils are insoluble, demonstrate poor antigenicity and resist enzymatic destruction[20]. This makes degradation of amyloid difficult, and once deposited in the tissues amyloid tends to persist[5]. The pathogenesis is unclear[8] but deposition of fibrils is likely to follow proteolytic cleavage of an abnormal precursor protein into subunits capable of polymerization into β pleated sheets[1].

Diagnosis

The diagnosis of amyloidosis is established by biopsy of either the main organ involved or a tissue in which amyloid is frequently deposited[11]. Rectal biopsies, which must include submucosa, are most commonly taken and are positive in 73–84 per cent of patients[6,7]. Other sites used include kidney and liver (positive in 90–96 per cent of cases)[7]; the skin[21], spleen[22], small intestine[23] gingiva[23], and subcutaneous abdominal wall fat[24] may also provide tissue for diagnosis. The type of fibril present may be ascertained using biochemical and immunological techniques[11]. When systemic amyloidosis is suspected the patient should also be investigated for an underlying plasma cell dyscrasia as multiple myeloma is found in 6–15 per cent of patients with primary amyloidosis[9].

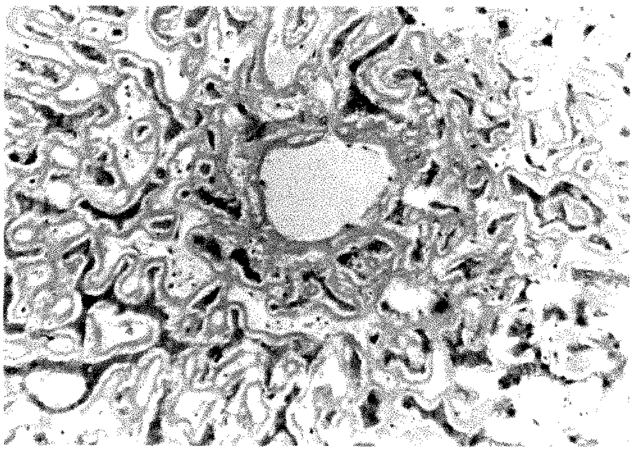

Figure 1 *Amyloidosis of the liver. The pale homogeneous amyloid substance is deposited along the walls of the sinusoids, enclosing the liver cells. Despite the resulting hepatocyte atrophy liver function is not usually severely impaired*

Prognosis and medical treatment

Localized amyloidosis is essentially a benign condition, recurrence rarely occurring following surgical excision[12]. Systemic amyloidosis, however, is almost invariably fatal and treatment is mainly supportive; death usually follows a cardiac event or renal failure[3].

Median survival in primary systemic amyloidosis lies between 12 and 15 months and most patients succumb within 3 years of the diagnosis[6]. In myeloma associated amyloidosis the outlook is even gloomier with a median survival of only 4 months[6]. The prognosis is better with secondary amyloidosis where survival up to 5 years[11] is common and there are occasional case reports documenting long term survival[25]. Patients in whom the initial presentation is with congestive cardiac failure have a poorer outlook than those without clinical evidence of cardiac disease[6].

Treatment of systemic amyloidosis remains unsatisfactory and includes immunosuppression by cytotoxic drugs to reduce the production of amyloid fibrils, and the use of agents to dissolve formed fibrils[3,20]. In the case of secondary amyloidosis treatment of the chronic inflammatory disease is clearly of importance[19,26]. Other approaches that have been suggested but not yet evaluated are the removal of amyloid precursors by plasmaphoresis or immunoabsorption, agents to prevent polymerization of amyloid fibrils, and the use of antisera to amyloid to promote phagocytosis[3].

Although amyloid has usually been regarded as an inert material there is some evidence that the body has systems capable of dissolving it, probably by tissue-based proteolytic enzymes[27]. Regression of amyloid has been documented following removal of the inciting agent[28], treatment of the underlying disorder[19] and very rarely, as a spontaneous event[29].

Only two drugs have been shown to be of consistent benefit. Colchicine, used prophylactically, prolongs survival and prevents acute attacks in systemic amyloidosis associated with familial mediterranean fever[30]. Chlorambucil improves survival and alleviates joint symptoms in amyloidosis associated with chronic juvenile arthritis[12,31]. Other drugs, such as melphalan and penicillamine, have been tried with conflicting results[12]. Dimethylsulphoxide (DMSO) has been shown to dissolve amyloid fibrils *in vitro* and to reduce the extent of amyloid in experimental animals[32,33]. In man, clinical improvement has been reported with DMSO but patient acceptability is low because it causes persistent malodour[12].

Presentation and treatment of surgical complications

Gastrointestinal

Amyloid may cause widespread damage of the gastrointestinal tract[34]. Involvement is common in both AL and AA types of amyloid (30–100 per cent)[23], hence the use of rectal, gingival and small intestinal biopsies in the diagnosis of systemic amyloidosis. Symptoms may be produced by direct involvement of the gastrointestinal tract or by infiltration of the autonomic nervous system[8]. Vascular deposits may cause intestinal ischaemia[35,36], haemorrhage[35,36] and perforation[37]; mucosal lesions may be associated with malabsorption[6]; and neuromuscular infiltration may produce a motility disorder[38]. In addition large deposits may act as a 'mass' lesion simulating a malignancy[39]. Surgical intervention should be cautious as there may be an associated haemorrhagic diathesis[40], and resection margins should be well clear of amyloid deposits or anastomotic dehiscence may follow poor local healing[41].

Macroglossia occurs in 20 per cent of patients with systemic AL and may occasionally be incapacitating[6]. In severe cases nasogastric or gastrotomy feeding will be required, as a partial glossectomy can be difficult in amyloidosis[7,11]. In the oesophagus, localized deposits may mimic carcinoma. Heitzman *et al.*[42] performed partial oesophagogastrectomy for a perforated middle/lower third lesion, and Solanke *et al.*[43] performed an antethoracic colon transplant for an irresectable lower third deposit. In each case the diagnosis of amyloidosis was made postoperatively. Both patients made good recoveries although the latter patient developed a cervical fistula that resolved spontaneously.

Deposits mimicking tumours have been reported elsewhere in the bowel. In the stomach 'tumours' may be localized deposits[44], or part of a generalized amyloidosis[45,46]. Shnider and Burka[45] reported a patient who developed a duodenal/gastric fistula and subsequently died following a partial gastrectomy for an amyloid 'tumour' causing complete pyloric obstruction. Pandarinath *et al.*[47] reported a case of massive small bowel amyloid mimicking multiple tumours who presented with abdominal pain and haematemesis. Nodules had been noted in the jejunum at a laparotomy 4 years before presentation and in retrospect biopsies were positive for amyloid. Colonic masses of amyloid have been described in the descending colon[41], sigmoid colon[39] and rectum[48], and usually present with rectal bleeding.

Amyloid is an uncommon complication of Crohn's disease[49] occurring in 1–8 per cent of cases[50]. Occasionally amyloidosis may present as a case of 'inflammatory bowel disease'[41]. Patients with Crohn's disease and amyloid usually present with renal involvement which progresses rapidly to renal failure[50]. Although it has been suggested that excision of the affected bowel may cause regression of amyloid[49] the results are poor. Rashid *et al.*[50] reviewed 28 cases of amyloid associated with Crohn's, 14 of whom underwent surgery. Six of the 14 patients died within 6 months of surgery from rapid worsening of renal function, and in only one case did amyloid regress.

Perforation through amyloid deposits is usually fatal. Griffel *et al.*[51] reported a 57-year-old man who underwent subtotal resection of his small bowel following intestinal perforation. Postoperatively he required total parenteral nutrition and was well 5 months after surgery. He was the first documented survivor of this complication of amyloid.

Amyloid neuropathy may produce severe constipation or diarrhoea with anal incontinence. Ek *et al.*[52] described three patients with primary neuropathic amyloidosis whose lives were transformed by the formation of an enterostomy. All were alive and well at 10, 18 and 20 months following surgery.

Involvement of the intestinal musculature may cause a pseudo-obstruction, with a poor outcome. Legge *et al.*[38] reviewed 15 patients with pseudo-obstruction secondary to amyloidosis, six of whom underwent operation for presumed mechanical obstruction. Five of these patients died in the immediate postoperative period, the sixth surviving for 9 months with a colostomy. Of the nine patients managed conservatively four apparently died from persistence or recurrence of pseudo-obstruction, one from a pulmonary embolus and four from cardiac/renal amyloid.

Peritoneal infiltration with amyloid may obstruct the alimentary tract by encasement. We have seen a patient with histologically proven primary amyloidosis who underwent multiple operations for the removal of peritoneal amyloid, and was alive at 14 years from the time of diagnosis. These deposits displayed unusually heavy calcification that was visible on plain abdominal radiographs (*Figure 2*).

Hepatomegaly occurs in 50 per cent of patients with systemic amyloidosis[15] but complications of hepatic involvement are uncommon. Portal hypertension producing varices may occur rarely. Kapp[53] reported a 46-year-old man with bleeding varices secondary to hepatic amyloid who died from persistent haemorrhage following a portacaval shunt. Although a coagulation defect was recognized it did not respond to fresh blood and fibrinogen, and it was believed that the continued bleeding may have been caused by impaired vascular contractility secondary to amyloid infiltration of the vessels.

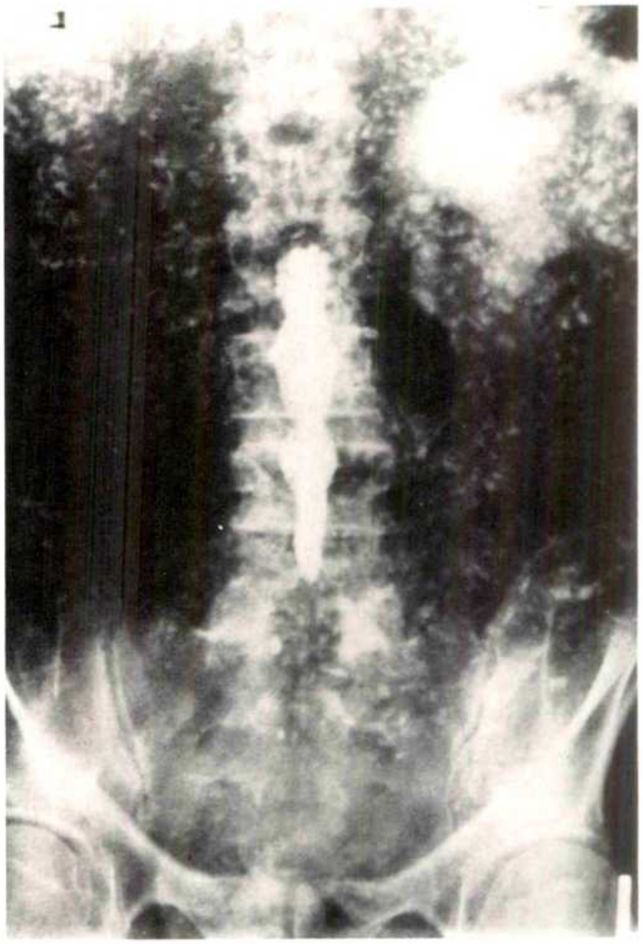

Figure 2 *Abdominal X-ray showing extensive calcification throughout peritoneal cavity due to amyloid deposits. Symptoms of intermittent intestinal obstruction have been relieved by local resection of amyloid deposits. There is also residual contrast from a myelogram previously undertaken for paraplegia. Recovery was complete following resection of amyloid deposits compressing the spinal cord*

Splenic involvement is usually asymptomatic. Splenomegaly occurs in 10–20 per cent[15] and may be massive. Spontaneous rupture may occur very rarely[54] and it is usually fatal. Splenectomy has been described as beneficial in the management of life threatening haemorrhage related to factor X deficiency[55].

Renal

Renal involvement is a common manifestation of systemic amyloidosis. Some 82–98 per cent[6,15] of patients will display a non-selective proteinuria at the time of diagnosis and in approximately one-third this will be severe enough to produce the nephrotic syndrome[6]. Typically there is a gradual deterioration in renal function ending in end stage renal failure. This is the cause of death of 43–65 per cent of patients with secondary amyloidosis, and in 16–25 per cent of patients with primary amyloidosis[15]. Uncommonly patients may present with nephrogenic diabetes insipidus or acute renal failure, which is usually secondary to renal vein thrombosis. Improvement in renal function has been reported as a spontaneous event[29] following treatment of the underlying disorder[19] and following therapy with cytotoxic drugs[56]. However, most patients with renal disease will inexorably deteriorate and documented regression is rare.

Few dialysis centres would now refuse to dialyse patients with amyloidosis[14] and in Europe approximately 0·5 per cent of registered haemodialysis patients are known sufferers[57]. Long term dialysis improves survival in both AL and AA types of amyloidosis[14] and reduces the incidence of painful crises in the amyloidosis associated with familial mediterranean fever[58].

Problems with access for haemodialysis may occur due to amyloid infiltration of the blood vessels but this may be overcome using PTFE vascular prostheses[59]. Jones[14] reported 29 patients who underwent haemodialysis for a mean of 19·4 months. Seven patients died during treatment, none of them from a renal cause.

Continuous ambulatory peritoneal dialysis (CAPD) has been advocated by some as an alternative to haemodialysis, but peritoneal deposits of amyloid may cause it to be unsuccessful[60]. Browning *et al.*[12] reported five patients who were alive and well at between 9 and 30 months from starting treatment with CAPD.

Increasing interest is being shown in the role of renal transplantation for end stage renal disease in amyloidosis[57,61,62]. Over 50 such transplants have now been performed with encouraging results. Transplantation appears to improve survival even in the presence of widespread disease and, although amyloid may be detected in the grafts at between 6 months and 4 years it seldom has clinical effects[14]. Dorman *et al.*[62] reported a patient who developed renal failure after a transplant due to amyloid deposition in the graft. This patient underwent a second transplantation 2 years after the first, with uneventful recovery.

Musculoskeletal

There are three distinct patterns of involvement of the musculoskeletal system which may present to the surgeon: synovial/articular; diffuse marrow infiltration; localized amyloidosis of bone[63].

In the first form amyloid may present with an arthropathy similar to rheumatoid arthritis[64]. This is often associated with periarticular soft tissue deposits, particularly around the shoulders. Carpal tunnel syndrome is a frequent complication of amyloid and is seen in over 20 per cent of cases of primary systemic amyloidosis; it requires surgical decompression[6,65]. Large subchondral cysts may develop in the femoral neck and pathological fractures have been reported through them[64]. In the axial skeleton diffuse marrow involvement may produce osteoporosis and painful compression fractures.

Localized amyloidosis of bone is a rare manifestation[66] in the absence of myeloma but has been reported in the sternum[67], vertebral column[68] and as multiple osteolytic deposits[67]. Paraplegia following spinal cord compression by amyloid tissue has been rarely described (*Figure 2*). McAnena *et al.*[68] described a 72-year-old woman who had an amyloid mass arising out of the sixth and seventh thoracic vertebrae; neurological signs improved dramatically after surgery but she died 4 months later in renal failure. Prasad *et al.*[69] described a 76-year-old woman in whom an extradural mass was excised without recurrence.

Head and neck

In the brain amyloid is typically laid down in and around the blood vessels[15]. Whether the fibrils are synthesized *in situ* or transplanted via the systemic circulation is unknown. Localized amyloid deposits are a frequent incidental finding at autopsy, and may also be associated with slow viral diseases, Alzheimer's dementia and congophilic angiopathy (primary cerebral amyloid angiopathy, a dementing disease of the elderly). Neurosurgeons may become involved in the management of patients with amyloid in two situations: to perform a brain biopsy as a diagnostic procedure in a patient with progressing dementia; and in the treatment of spontaneous intracerebral haematomas[70].

Amyloid angiopathy may account for up to 2 per cent of spontaneous intracerebral haematomas[71]. Although most cases appear to be sporadic, familial forms of amyloid with a high incidence of this complication have been reported from Japan, Europe and, in particular, Iceland. Gudmundsson *et al.*[17] reported a family with the Icelandic type of heredofamilial neuropathic amyloid with cerebral haemorrhage occuring in 22 out of 117 individuals over four generations. Cerebral haemorrhage was the cause of death in 19 individuals, accounting for 54·3 per cent of all deaths. In the fourth generation the mean age at death was 22·5 years. Recurrent haemorrhage is common, but surgery remains a mainstay of treatment despite the poor prognosis.

Amyloid is commonly found in the thyroid gland in systemic amyloidosis but rarely in amounts sufficient to cause a goitre[72]. Despite widespread infiltration of the gland clinical evidence of myxoedema is rare and usually follows thyroidectomy. The major significance of amyloid in the thyroid is in its resemblance to medullary carcinoma on needle biopsy of the gland.

Amyloid deposits in the eye may produce vitreous opacities or glaucoma. Pars plana vitrectomy may successfully restore vision[73,74], although the procedure may need repetition if the initial excision is incomplete[75].

There are over 300 reported cases of head and neck amyloid, usually in the form of localized deposits. The majority occur in the larynx (75 per cent), trachea, pharynx and tongue[76]. Localized tumours have been described in the maxillary sinus[76] and in the oral cavity[77] where they may mimic squamous cell carcinomas. Local excision is usually curative.

Respiratory

Amyloid deposits in the upper respiratory tract are well recognized and usually occur as localized 'tumours'[78-80]. Symptoms occur due to the mechanical effects of the tumour, and depend on the size and location of the lesion[78]. Characteristically cough, dyspnoea, wheezing and asthma in the presence of a normal chest radiograph occur in the initial stages, followed by haemoptysis (in 50 per cent), chronic bronchitis and repeated chest infections. Diagnosis may be surprisingly difficult to make as the radiographic and endoscopic appearances often mimic carcinoma[81]. Localized swellings can be removed endoscopically[78], and if excised completely they do not recur. More diffusely infiltrating lesions may require a laryngofissure approach in order to excise as much affected tissue as possible. Where such an approach is used Watanabe *et al.*[80] suggest that a split thickness skin graft is applied to the denuded area in order to prevent stenosis and prevent recurrence of the amyloid tumour.

In the lower respiratory tract amyloid is more common and presents in three forms[82]: diffuse interstitial deposits which resemble pulmonary oedema radiographically and are untreatable; single or multiple pulmonary nodules; and tracheobronchial deposits. Pulmonary nodules have a relatively benign nature and can be managed conservatively if the diagnosis of amyloid is made with certainty. However, the nodules are usually situated in the periphery and, despite the use of guided needle aspiration and transbronchial biopsies, surgical resection is often required to obtain a satisfactory result[83]. Tracheobronchial deposits are the commonest form of respiratory amyloid, and may occur as nodules or submucosal plaques. Intermittent bronchoscopic resection is the usual method of treatment[84], although laryngofissure or tracheal resection may occasionally be required. Breuer *et al.*[82] reported two patients with symptomatic localized tracheobronchial amyloid deposits treated by repeated carbon dioxide laser photoresection. In both cases symptoms were relieved, and lung function improved, but one patient required a temporary tracheostomy because of subglottic oedema. Submucosal plaques are more difficult to cure due to their diffuse nature and may be associated with severe haemoptysis. Thompson and Citron[83] suggest that carbon dioxide laser photoresection may prove to be the treatment of choice in this situation.

Miscellaneous

Cutaneous involvement is frequent in primary and myeloma associated amyloidosis, and may occasionally be seen in secondary amyloidosis[3]. Surgery plays little role in the management of the cutaneous amyloidoses, despite medical treatment being unsatisfactory. Wong and Li[85] described the use of dermabrasion for lichen amyloidosis, with good results after a 5-year follow-up. It relieved itching associated with the lesions and produced minimal scarring, although some degree of hyper- or hypopigmentation was common. Deposits in the *breasts* are extremely rare. Sadeghee and Moore[86] reported a case of secondary amyloidosis complicated by cutaneous nodules and bilateral amyloid tumours of the breasts. These resembled calcified fibroadenomata on mammography and the diagnosis was made by incisional biopsy.

Amyloidosis of the *bladder* is usually in the form of localized deposits. These tend to cause painless haematuria or an obstructive uropathy. The main danger is that inappropriate radical surgery may be undertaken in the belief that the lesion is a carcinoma[87]. Bodner *et al.*[88] reported a 21-year-old man who presented with primary amyloidosis of the glans penis and *urethra*. This is a rare manifestation of amyloidosis and excision of the deposit necessitated a reconstruction of the urethra. Three years following surgery there was no evidence of recurrence. Weinrauch *et al.*[89] described a 57-year-old female with widespread deposition of amyloid in serosal membranes causing encasement of the heart, *ureters* and gastrointestinal tract. She required four operations over 2 years to maintain urinary drainage but eventually developed renal failure and died from a gastrointestinal haemorrhage. At one stage she had presented with cardiac tamponade which was relieved by open drainage of the pericardium.

Cardiac involvement is very common in the acquired systemic amyloidoses[15] and is a major cause of death in most series. Pacemakers may need to be inserted for conduction disturbances and cardiac transplantation may be successfully undertaken in selected patients with amyloid cardiomyopathy.

Although considerable progress has been made in understanding the pathogenesis of amyloidosis in the last 25 years, medical treatment remains unsatisfactory. Surgery plays an important role in the management of systemic and localized amyloidosis. When surgical complications arise, operative intervention must always be considered seriously as the results are usually rewarding despite the limited and uncertain long term prognosis.

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References

1. Franklin EC, Gorevic PD. The Amyloid Diseases. In: Fougereau M, Dausset J, (eds) *Immunology 80 – Progress in Immunology IV.* London: Academic Press, 1980, 1219–30.
2. Gorevic PD, Franklin EC. Amyloidosis. *Ann Rev Med* 1981; **32**: 261–71.
3. Breathnach SM, Black MM. Systemic amyloidosis and the skin: a review with special emphasis on clinical features and therapy. *Clin Exp Dermatol* 1979; **4**: 517–36.
4. Glenner CG. Amyloid deposits and amyloidosis. *N Eng J Med* 1980; **302**: 1283–92; 1333–43.
5. Hind CRK, Pepys MB. Amyloidosis: classification and pathogenesis. *Hospital Update* 1984; **10**: 593–8.
6. Kyle RA, Greipp PR. Amyloidosis (A) – clinical and laboratory features in 229 cases. *Mayo Clinic Proc* 1983; **58**: 665–83.
7. Kyle RA, Bayrd ED. Amyloidosis: review of 236 cases. *Medicine (Baltimore)* 1975; **54**: 271–99.
8. Cohen AJ. An update of clinical, pathologic and biochemical aspects of amyloidosis. *Int J Dermatol* 1981; **20**: 515–30.
9. Cohen AJ. Amyloidosis. *N Engl J Med* 1967; **277**: 522–30, 574–83; 628–38.
10. Hind CRK, Caspi P, Collins PM, Baltz ML, Pepys MB. Specific chemical dissociation of fibrillar and non fibrillar components of amyloid deposits. *Lancet* 1984; **ii**: 376–8.
11. Hind CRK, Pepys MB. Amyloidosis: diagnosis, prognosis and treatment. *Hospital Update* 1984; **10**: 737–48.
12. Browning MJ, Banks RA, Tribe CR, Hollingworth P, Kingswood C, MacKenzie JC, Bacon PA. Ten year's experience of an amyloid clinic. A clincopathological survey. *Q J Med* 1985; **54**: 213–27.
13. Lender M. Amyloidosis associated with neoplastic diseases. *S Afr Med J* 1974; **48**: 1944–6.
14. Jones NF. Renal amyloidosis: pathogenesis and therapy. *Clin Nephrol* 1976; **6**: 459–64.
15. Hind CRK, Pepys MB. Amyloidosis: clinical features. *Hospital Update* 1984; **10**: 637–48.
16. Anderson R, Hofer P-Å. Genitourinary disturbances in familial and sporadic cases of primary amyloidosis with polyneuropathy. *Acta Med Scand* 1974; **195**: 49–58.
17. Gudmundsson G, Hallgrimsson J, Jonasson TA, Bjarnason O. Hereditary cerebral haemorrhage with amyloidosis. *Brain* 1972; **95**: 387–404.
18. Pirani CL. Tissue distribution of amyloid. In: Wegelius O, Pasternack A (eds). *Amyloidosis.* London: Academic Press, 1976, 33–49.
19. Triger DR, Joekes AM. Renal amyloidosis – a fourteen year follow up. *Q J Med* 1973; **42**: 15–40.
20. Wegelius O. The place of amyloidosis in experimental and clinical medicine. In: Wegelius O, Pasternack A, eds. *Amyloidosis.* London: Academic Press, 1976, 1–13.
21. Rubinow A, Cohen AJ. Skin involvement in generalised amyloidosis: A study of clinically involved and uninvolved skin in 50 patients with primary and secondary amyloidosis. *Ann Intern Med* 1978; **88**: 781–5.
22. Pasternack A. Fine needle aspiration biopsy of the spleen in the diagnosis of systemic amyloidosis. In: Wegelius O, Pasternack A, eds. *Amyloidosis.* London: Academic Press, 1976, 393–9.
23. Pettersson T. Intestinal amyloidosis. In: Wegelius O, Pasternack A, eds. *Amyloidosis.* London: Academic Press, 1976, 447–53.
24. Libbey CA, Skinner M, Cohen AJ. Use of abdominal fat tissue aspirate in the diagnosis of systemic amyloidosis. *Arch Intern Med* 1983; **143**: 1549–52.
25. Crow KD. Primary amyloidosis. *Brit J Dermatol* 1977; 97(Suppl 15): 58–60.
26. Karsenty G, Ulmann A, Droz D, Carnot F, Grünfeld J-P. Clinical and histological resolution of systemic amyloidosis after renal cell carcinoma removal. *Nephron* 1985; **40**: 232–4.
27. Waldenström J. Reversibility and constancy of amyloidosis. In: Wegelius O, Pasternack A, eds. *Amyloidosis.* London: Academic Press 1976, 543–52.
28. Shirahama T, Cohen AJ. Redistribution of amyloid deposits. *Am J Pathol* 1980; **99**: 539–50.
29. Michael J, Jones NF. Spontaneous remissions of nephrotic syndrome in renal amyloidosis. *Br Med J* 1978; **i**: 1592–3.
30. Ravid M, Robson M, Kedar I. Prolonged colchicine treatment in four patients with amyloidosis. *Ann Intern Med* 1977; **87**: 568–70.
31. Bywaters EGL, Ansell BM. Amyloidosis in the chronic rheumatic diseases. In: Wegelius O, Pasternack A eds. *Amyloidosis.* London: Academic Press, 1976, 409–17.
32. Isobe T, Osserman EF. Effects of dimethysulfoxide (DMSO) on Bence Jones proteins, amyloid fibrils and casein-induced amyloidosis. In: Wegelius O, Pasternack A, eds. *Amyloidosis.* London: Academic Press 1976, 247–57.
33. Hanai N, Ishihara T, Uchino F, Imada N, Fujihara S, Ikegami J. Effects of dimethylsulfoxide and calchicine on the resorption of experimental amyloid. *Virchows Arch (Pathol Anat)* 1979; **384**: 45–52.
34. Gilat T, Revach M, Sohar E. Deposition of amyloid in the gastrointestinal tract. *Gut* 1969; **10**: 98–104.
35. Brom B, Bank S, Marks IN, Milner G, Baker P. Ischaemic colitis, gastric ulceration and malabsorption in a case of primary amyloidosis. *Gastroenterology* 1969; **57**: 319–23.
36. Mallory A, Struthers JE, Kern F. Persistent hypotension and intestinal infarction in a patient with primary amyloidosis. *Gastroenterology* 1975; **68**: 1587–92.
37. Ioachim N-J, McKenna PJ, Delaney WE, Toth I, Chung FJ. Cryoglobulinaemia with amyloidosis associated with intestinal lymphoma. *Arch Intern Med* 1978; **138**: 1158–60.
38. Legge DA, Wollaeger EE, Carlson HC. Intestinal pseudo-obstruction in systemic amyloidosis. *Gut* 1970; **11**: 764–7.
39. Bergman F. Amyloid 'tumour' in sigmoid colon. *Acta Path Microbiol Scand (A)* 1962; **55**: 395–400.
40. Yood RA, Skinner M, Rubinow A, Talarico L, Cohen AJ. Bleeding manifestations in 100 patients with amyloidosis. *J Am Med Assoc* 1983; **249**: 1322–4.
41. Johnson DH, Guthrie TH, Tedesco FJ, Griffen JW, Anthony HF. Amyloidosis masquerading as inflammatory bowel disease with a mass lesion simulating a malignancy. *Am J Gastroenterol* 1982; **77**: 141–5.
42. Heitzman EJ, Heitzman GC, Elliot CF. Primary esophageal amyloidosis. *Arch Intern Med* 1962; **109**: 595–600.

43. Solanke TF, Olurin EO, Nwakonobi F, Udeozo IOK. Primary amyloid tumour of the oesophagus treated by colon transplant. *Br J Surg* 1967; **54**: 943–6.
44. Intriere AD, Brown CH. Primary amyloidosis – Report of a case of gastric involvement only. *Gastroenterology* 1956; **30**: 833–8.
45. Shnider BI, Burka P. Amyloid disease of the stomach simulating gastric carcinoma. *Gastroenterology* 1955; **28**: 424–30.
46. Williams RR, Baggenstoss AH. Amyloid tumour of the stomach. *Cancer* 1952; **5**: 249–53.
47. Pandarinath GS, Levine SM, Sorokin JJ, Jacoby JH. Selective massive amyloidosis of the small intestine mimicking multiple tumours. *Radiology* 1978; **129**: 609–10.
48. Williamson RCN. Primary amyloidosis of the rectum. *Proc R Soc Med* 1972; **65**: 10.
49. Fitchen JH. Amyloidosis and granulomatous ileocolitis. Regression after surgical removal of the involved bowel. *N Eng J Med* 1975; **292**: 352–3.
50. Rashid H, Blake D, Gokal R, Gooptu D, Kerr DNS. The association of renal amyloidosis with regional enteritis (Crohn's disease) – report of two cases and review of the literature. *Clin Nephrol* 1980; **14**: 154–7.
51. Griffel B, Man B, Kraus L. Selective massive amyloidosis of small intestine. *Arch Surg* 1975; **110**: 215–17.
52. Ek BO, Holmlund DEW, Sjo Din J-G, Steen LE. Enterostomy in patients with primary neuropathic amyloidosis. *Am J Gastroenterology* 1978; **70**: 365–70.
53. Kapp JP. Hepatic amyloidosis with portal hypertension. *J Am Med Assoc* 1965; **191**: 153–5.
54. Polliack A, Hershko C. Spontaneous rupture of the spleen in amyloidosis. *Isr J Med Sci* 1972; **8**: 57–60.
55. Greipp PR, Kyle RA, Bowie EJW. Factor X deficiency in primary amyloidosis: resolution after splenectomy. *New Engl J Med* 1979; **301**: 1050–51.
56. Kyle RA, Wagoner RD, Holley KE. Primary systemic amyloidosis – resolution of the nephrotic syndrome with melphalan and prednisolone. *Arch Intern Med* 1982; **142**: 1445–47.
57. Gurland HJ, Brunner FP, Ghansher C *et al.* Combined report on regular dialysis and transplantation in Europe, VI, 1975. In: Robinson BHB, Vereerstraesen P, Hawkins JE, eds. *Dialysis, Transplantation, Nephrology: Proceedings of the European Dialysis and Transplantation Association.* Bath, England: Pitman Press, 1976; **13**: 22–25.
58. de Wardener HE. In: *The Kidney* (5th edn) Edinburgh, Churchill Livingstone. 1985, 521–6.
59. Suzuki H, Konoshi K, Izumi Y, Saruta T, Ozawa Y, Kato E. Long term haemodialysis in a patient with primary amyloidosis, renal failure, and avascular necrosis of the femoral heads. *South Med J* 1982; **75**: 1018–20.
60. Lawrence CA. Amyloid deposition makes peritoneal dialysis ineffective. (letter) *J R Soc Med* 1984; **77**: 895.
61. Cohen AJ, Bricetti AB, Harrington JT, Mannick AJ. Renal transplantation in two cases of amyloidosis. *Lancet* 1971; **ii**: 513–16.
62. Dorman SA, Gamelli RL, Benziger JR, Trainer TD, Foster RS. Systemic amyloidosis involving two renal transplants. *Hum Pathol* 1981; **12**: 735–8.
63. Goldman AB, Pavlov H, Bullough P. Case report 137: Primary amyloidosis involving the skeletal system. *Skeletal Radiol* 1981; **6**: 69–74.
64. Hall S, Luthra HS. Rheumatological manifestations of amyloid disease. *Minn Medicine* 1983; **66**: 631–2.
65. Chapman RH, Lotter F. The carpal tunnel and amyloidosis. *Clin Orthop* 1982; **169**: 159–62.
66. Delaney-Baxter MP, Lenczner E, Armstrong GWD. Orthopaedic manifestations of amyloidosis. *J Bone Jt Surg* 1985; **67-B**: 328 (Abstract).
67. Mulder JD, van Rijssel ThG. Case report 233. *Skeletal Radiol* 1983; **10**: 53–55.
68. McAnena OJ, Feely MP, Kealy WF. Spinal cord compression by amyloid tissue. *J Neurol Neurosurg Psychiatry* 1982; **45**: 1067–9.
69. Prasad BK, Andrews K, Dutton J, Reid H. Localized amyloid deposit producing paraplegia. *Br Med J* 1981; **283**: 1087.
70. Rengachary SS, Racela LS, Watanabe I, Abdou N. Neurosurgical and immunological implications of primary cerebral amyloid (congophilic) angiopathy. *Neurosurgery* 1980; **7**: 1–9.
71. Jellinger K. Cerebrovascular amyloidosis with cerebral haemorrhage. *J Neurol* 1977; **214**: 195–206.
72. James PD. Amyloid goitre. *J Clin Pathol* 1972; **25**: 683–8.
73. Kasner D, Miller GR, Taylor WH, Sever RJ, Norton EWD. Surgical treatment of amyloidosis of the vitreous. *Tr Am Acad Ophthal Otolaryng* 1968; **72**: 410–18.
74. Van Rens GHMB, Doubois HF, Winkelman JE. Para plana vitrectomy in a case of amyloidosis of the vitreous. *Doc Ophthalmol* 1985; **59**: 45–9.
75. Irvine AR, Char DH. Recurrent amyloid involvement in the vitreous body after vitrectomy. *Amer J Ophthalmol* 1976; **82**: 705–708.
76. Denneny JC, Weisman RA, Marlowe FL. Primary amyloidosis of the maxillary sinus. *Trans Pa Acad Ophthalmol Otolaryngol* 1984; **37**: 79–81.
77. Rennie JS, Critchlow HA. Solitary oral amyloid – a report of two cases. *Int J Oral Surg* 1982; **11**: 73–6.
78. Shaw H. Tumours of the larynx. In: Ballantyne J, Groves J, eds. *Diseases of the Ear, Nose and Throat.* Vol 4. 4th ed. London: Butterworths 1979, 432–3.
79. Finn DG, Farmer JC. Management of amyloidosis of the larynx and trachea. *Arch Otolaryngol* 1982; **108**: 54–6.
80. Watanabe H, Makishima K, Komiyama S, Hiroto I. Surgical treatment of the laryngo-tracheal amyloidosis. *Auris Nasus Larynx (Tokyo)* 1984; **11**: 157–62.
81. Naef AP, Savary M, Schmid de Grüneck JM, Baumann GP. Amyloid pseudotumour treated by tracheal resection. *Ann Thorac Surg* 1977; **23**: 578–81.
82. Breuer R, Simpson GT, Rubinow A, Skinner M, Cohen AJ. Tracheobronchial amyloidosis: treatment by carbon dioxide laser photoresection. *Thorax* 1985; **40**: 870–71.
83. Thompson PJ, Citron KM. Amyloid and the lower respiratory tract. *Thorax* 1983; **38**: 84–7.
84. Flemming AFS, Fairfax AJ, Arnold AG, Lane DJ. Treatment of endobronchial amyloidosis by intermittent bronchoscopic resection. *Br J Dis Chest* 1980; **74**: 183–8.
85. Wong C-K, Li W-M. Dermabrasion for lichen amyloidosis. *Arch Dermatol* 1982; **118**: 302–304.
86. Sadaghee SA, Moore SW. Rheumatoid arthritis, bilateral amyloid tumours of the breast, and multiple cutaneous amyloid nodules. *Am J Clin Pathol* 1974; **62**: 472–6.
87. Missen GAK, Tribe CR. Catastrophic haemorrhage from the bladder due to unrecognised secondary amyloidosis. *Br J Urol* 1970; **42**: 43–9.
88. Bodner H, Retsky MI, Brown G. Primary amyloidosis of glans penis and urethra: resection and reconstruction. *J Urol* 1981; **125**: 586–8.
89. Weinrauch LA, Desautels RE, Christlieb AR, Kaldany A, D'Elia JA. Amyloid deposition in serosal membranes: its occurrence with cardiac tamponade, bilateral ureteral obstruction and gastrointestinal bleeding. *Arch Intern Med* 1984; **144**: 630–2.

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Review

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Cystic adventitial arterial disease

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Cystic adventitial disease (CAD) was first reported in 1947 by Atkins and Key[1]. They recorded the case of a 40-year-old man with intermittent claudication associated with a palpable swelling above the inguinal ligament. At operation a cyst was dissected from the external iliac artery and was described as a typical ganglion.

The first report of involvement of the popliteal artery was made by Ejrup in 1954[2], who suggested that the aetiology was mucoid degeneration of the media. The world literature has been reviewed by Flanigan on three occasions, most recently in 1979[3]. Of the 115 cases he studied, the popliteal artery was affected in 85 per cent. CAD has also been described in the external iliac, femoral[4], radial and ulnar arteries[5], and in branches of the popliteal artery[6]. The adjacent vein has been involved on three occasions.

The incidence of CAD is approximately 1:1200 claudicants[7] or 1:1000 of those undergoing arteriography[8]. About 85 per cent of cases are male, and the average age at presentation is 42 years[3], (range 11–70 years)[9,10].

Aetiology

The cause of the deposition of gelatinous material between the adventitia and media of an arterial wall is not known, but several theories have been suggested. Simple degeneration is unlikely since the condition has been described in childhood[6,10], and there is no association with any generalized connective tissue disorder[11].

The affected vessel is commonly closely related to a joint, and repeated flexing of the arterial wall might induce activity in dormant mucin-secreting cells[12]. However this too is unlikely because biochemically the mucin is of the nature of ground substance rather than epithelial secretion[13]. If microtrauma were the cause, then CAD would be expected to occur both more often[14], and on occasions bilaterally.

The most popular belief is that the cyst is a true ganglion arising from an adjacent joint capsule or tendon sheath[15] and, as with ganglia elsewhere, a direct communication with the joint need not persist[16].

Presentation

Intermittent claudication is the presenting feature. The onset is characteristically abrupt, possibly due either to sudden rupture of the cyst[17] or to haemorrhage within it[2], and this may suggest the correct diagnosis in older patients[18]. On examination there are usually no stigmata of generalized arterial disease and only rarely is the cyst palpable. When the vessel is only partially occluded, peripheral pulses may be present with the limb extended but disappear during joint flexion[19], and a bruit may be audible[20].

The typical arteriographic appearance is of a smooth stenosis or an occlusion of a single vessel in an otherwise normal arterial tree. If the cyst encircles the artery the stenosis is symmetrical (*Figure 1*), but when eccentrically placed a curvilinear defect is seen, the 'scimitar sign' (*Figure 2*). Recent reports stress the value of ultrasound[21] and computerized tomography[22] in confirming the diagnosis. Conditions to be considered in the differential diagnosis include atherosclerosis, embolism, popliteal artery entrapment syndrome and thrombosis of a popliteal artery aneurysm.

Management

Almost all cases reported in the literature have been treated surgically and the results are excellent. When the vessel is not occluded then simple cyst excision is an acceptable treatment because the intima and media are usually spared in CAD. Needle aspiration of the cyst at operation has also been reported on two occasions[23]. The essential criteria for success with either of these procedures is the immediate restoration of normal distal flow. Additional patchplasty has been recommended when a stenosis

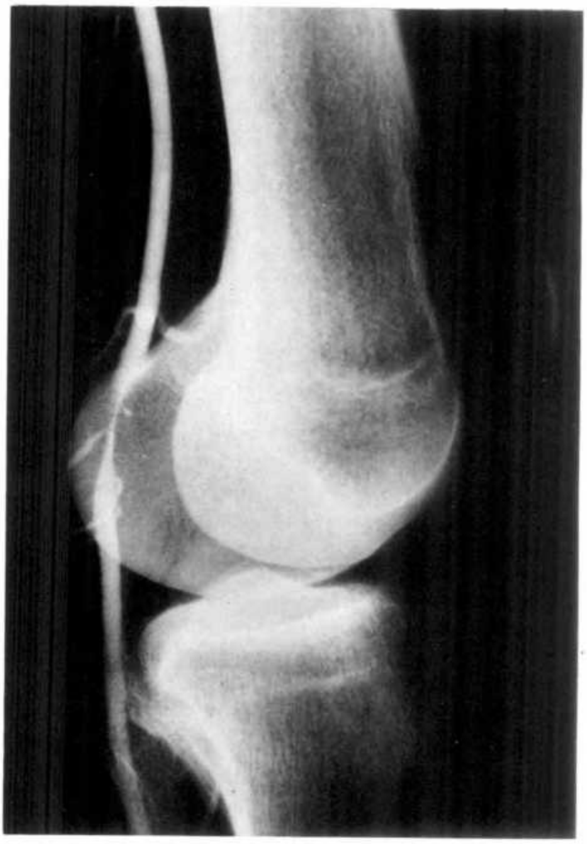

Figure 1 *Symmetrical smooth-walled stenosis of the popliteal artery due to CAD*

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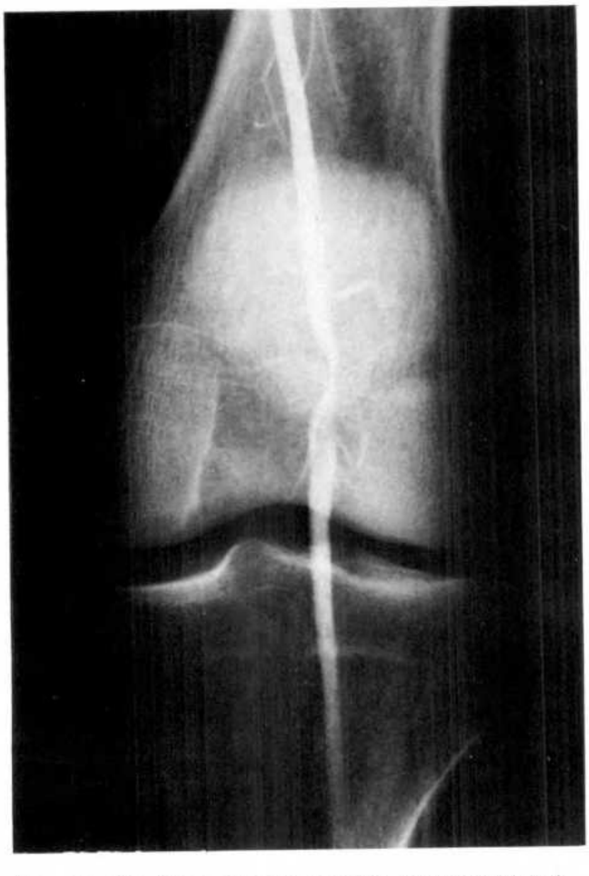

Figure 2 *Curvilinear defect due to CAD. The 'scimitar sign'*

remains but, although short term results are good, this operation is prone to aneurysm formation and is best avoided[3].

In 30 per cent of cases there is complete arterial occlusion and further measures are needed. Occasionally, resection with direct end-end anastomosis is possible[24], but more commonly bypass grafting is required.

Opinion is divided as to the best method of treatment for patent vessels affected by CAD, and paucity of cases precludes controlled trials. Flanigan found the two procedures employed to be equally successful; of 41 cases treated by cyst excision alone 4 (9·7 per cent) developed recurrent symptoms, and of 30 treated by resection and vein graft only 2 failed (6·6 per cent). The results from bypass grafting are not adversely affected by incomplete excision of the cyst, and good graft flows have been recorded up to 30 years later[25]. As might be expected, results are better with autogenous vein grafts than with prosthetic materials. In our experience of five cases, bypass grafting is often considerably easier than cyst excision because of the degree of fibrosis surrounding the cyst and its adherence to the neighbouring joint capsule.

There have been a few isolated reports of conservative treatment. Percutaneous transluminal angioplasty has been shown to be unsuccessful[26] because, unlike the situation in atherosclerosis, the intima in CAD is usually normal and the cyst wall is compliant. There are two recent reports of CT-directed percutaneous cyst aspiration, and in both cases distal flow was re-established. In one, the cyst contents were successfully evacuated[22], but in the other no material was aspirated and exploration was therefore performed[27]. It transpired that the cyst contents had extravasated following needle puncture and no further procedure was required. These early reports are encouraging although in neither case has follow-up exceeded one year. Even if relief of symptoms is only transient there may be considerable long term benefit in delaying the need for a bypass graft in a young patient.

Overall, the long term results are much better than for patients with atherosclerosis. Of 106 operative procedures reviewed[3], 2 patients had residual claudication and one other ultimately required an amputation. There are no reports of the development of the disease in a second vessel.

References

1. Atkins HJB, Key JA. A case of myxomatous tumour arising in the adventitia of the left external iliac artery. *Br J Surg* 1947; **34**: 426–7.
2. Ejrup B, Hierton T. Intermittent claudication. Three cases treated by a free graft. *Acta Chir Scand* 1954; **108**: 217–30.
3. Flanigan DP, Burnham SJ, Goodreau JJ, Bergan JJ. Summary of cases of adventitial cystic disease of the popliteal artery. *Ann Surg* 1979; **189**: 165–75.
4. Hildreth DH. Cystic adventitial disease of the common femoral artery. *Am J Surg* 1975; **130**: 92–6.
5. Parkes A. Intranerval ganglion of the lateral popliteal nerve. *J Bone Jt Surg* 1961; **43B**: 784–90.
6. Lewis GJT, Douglas DM, Reid W, Kennedy Watt J. Cystic adventitial disease of the popliteal artery. *Br Med J* 1967; **3**: 411–15.
7. Anon. Cystic degeneration of the popliteal artery. *Br Med J* 1970; **4**: 699–700.
8. Linquete M, Mesmacque R, Beghin B *et al.* Degenerescence kystique de l'adventice de l'artere poplitee. *Sem Hosp Paris* 1967; **43**: 3005–13.
9. Harris JD, Jepson RP. Cystic degeneration of the popliteal artery. *Aust NZ J Surg* 1965; **34**: 265.
10. Zinicola N, Ferrero S, Odero A. Adventitial cyst of the popliteal artery. Case report. *Minerva Cardioangiol* 1973; **21**: 474–86.
11. Haid SP, Conn J, Bergan JJ. Cystic adventitial disease of the popliteal artery. *Arch Surg* 1970; **101**: 765–70.
12. Little JM, Goodman AH. Cystic adventitial disease of the popliteal artery. *Aust NZ J Surg* 1967; **57**: 708–13.
13. DeLaurentis DA, Wolferth CC, Wolf FM *et al.* Mucinous adventitial cysts of the popliteal artery in an 11 year old girl. *Surgery* 1973; **74**: 456–9.
14. Savage PEA. Arterial cystic degeneration. *Postgrad Med J* 1972; **48**: 603–8.
15. Shute K, Rothie NG. Aetiology of cystic arterial diease. *Br J Surg* 1973; **60**: 397–400.
16. McCevedy BV. Simple gangia. *Br J Surg* 1962; **49**: 585–94.
17. Taylor H, Taylor RS, Ramsay CA. Cyst of popliteal artery (letter). *Br Med J* 1967; **4**: 109–10.
18. Hall R, Proud G, Chamberlain J, McNeil IF. Cystic adventitial disease of the common femoral and popliteal arteries. *Br J Surg* 1985; **72**: 756–8.
19. Ishikawa K, Mishima Y, Kobayashi S. Cystic adventitial disease of popliteal artery. *Angiology* 1961; **12**: 357–66.
20. Eastcott HHG. Cystic myxomatous degeneration of the popliteal artery (letter). *Br Med J* 1963; **2**: 1270.
21. Wilbur AC, Woefel GF, Meyer JP, Flanigan DP, Spigos DG. Adventitial cystic disease of the popliteal artery. *Radiology* 1985; **155**: 63–4.
22. Deutsch AL, Hyde J, Miller SM, Diamond CG, Schanche AF. Cystic adventitial degeneration of the popliteal artery: CT demonstration and directed percutaneous therapy. *Am J Roentgenol* 1985; **145**: 117–18.
23. Mentha C. Degenerescence kystique adventitielle ou bursite de l'artere poplitee. *J Chirur* 1965; **89**: 173–80.
24. Tracy GD, Ludbrooke J, Rundle FF. Cystic adventitial disease of the popliteal artery. *Vasc Surg* 1969; **3**: 10–17.
25. Hierton T, Hemmingsson A. The autogenous vein graft as popliteal artery substitute. *Acta Chir Scand* 1984; **150**: 377–83.
26. Fox RL, Kahn M, Alder J *et al.* Adventitial cystic disease of the popliteal artery: Failure of percutaneous transluminal angioplasty as a therapeutic modality. *J Vasc Surg* 1985; **2**: 464–7.
27. Wilbur AC, Spigos DG. Case report. Adventitial cyst of the popliteal artery: CT-guided percutaneous aspiration. *J Compt Assist Tomogr* 1986; **10**: 161–3.

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Popliteal artery trauma: a high risk injury

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The clinical presentation and management of 28 popliteal artery injuries following penetrating and blunt trauma during a 6 year period is reviewed. Clinical and Doppler evaluation identified an arterial injury in 24 (85 per cent) patients. In eight (29 per cent) patients with arteriovenous fistulae or false aneurysms, pedal pulses were palpable during initial assessment. Three (10·7 per cent) patients had limb amputation attributable to delayed vascular repair, crush injury and sepsis. End-to-end arterial repair following blunt trauma resulted in early failure with thrombosis in two patients. Autogenous vein grafting was used in 12 patients and is advocated in all blunt popliteal arterial injuries. Routine repair of associated venous injuries and liberal criteria for early fasciotomy were used. Exoskeletal fixation or skeletal traction for compound and comminuted fractures is recommended for simplicity of application and wound management. The significant functional orthopaedic disability following blunt arterial trauma at the knee is emphasized.

Keywords: Popliteal arterial injury, vascular repair

Failure to restore vascular continuity following popliteal artery injury is a major cause of amputation in the young adult. Recognition of the critical factors influencing successful post-traumatic vascular repair has increased limb salvage and lessened morbidity[1]. Early diagnosis, reduced ischaemic time, selective use of arteriography, fasciotomy and repair of venous injuries are established practice. However, the management of associated skeletal and soft tissue injury and the role of intra-operative shunting or extra-anatomic bypass grafting are less clearly defined. This report evaluates our experience in treating 28 cases of popliteal artery trauma.

Patients and methods

Twenty-eight patients with popliteal arterial trauma were treated at Groote Schuur Hospital, Cape Town during the 6 year period from 1979 to 1984. There were 25 males and 3 females, ranging in age from 13 to 64 years (mean 30·1 years). Twenty-three (82 per cent) patients were younger than 35 years. Penetrating injuries due to low velocity gunshot injuries (10), knife-stabs (4) and shotgun injuries (2) were present in 16 patients. Pedestrian, car, motor cycle and maritime accidents (10) and assault (2) accounted for blunt injuries in 12 patients.

Clinical evidence of distal ischaemia, false aneurysm formation, arteriovenous fistula with a bruit, popliteal haematoma and arterial bleeding suggested vascular injury in 24 (85 per cent) patients (*Table 1*). Digital emboli originating in a popliteal false aneurysm was the presenting feature in one patient. In three patients with penetrating trauma in the popliteal fossa and no clinical or Doppler evidence of vascular injury the diagnosis was made on angiography (*Figure 1*). Eight patients with popliteal arterial injury had palpable pedal pulses on initial evaluation. Major associated cardiothoracic, visceral, vascular and remote skeletal injuries were present in four patients.

Two distinct clinical presentations were identified. Acute arterial trauma following recent injury was present in 21 patients; 18 patients in this group had signs of limb ischaemia with absent pulses and median 3 h (range, 2–48 h) ischaemic time. In the second group, comprising distant referrals, seven patients presented at intervals ranging from 4 days to 6 years following injury. Arteriovenous fistulae (4) or false aneurysms (3) were found in this late group. All had palpable pedal pulses while one patient presented with digital emboli distal to a popliteal false aneurysm 6 years after a stab wound (*Figure 2*). Associated local injuries in the popliteal area were present in 23 (82 per cent) patients. Combined popliteal arterial and venous injuries occurred in 12 patients. Popliteal venous injury was found in 12 of 16 (75 per cent) penetrating wounds; no venous damage occurred in the blunt injury group. Six patients had peripheral nerve deficit. Skeletal and joint injury was found in 12 patients and 14 patients had extensive soft tissue trauma (*Table 2*).

Pre-operative angiography was performed in 20 (71 per cent) patients. Operative repair in the ischaemic group was performed within 4 h following injury in four (19 per cent) patients, from 4 to 6 h in thirteen (62 per cent) and >6 h in four (19 per cent) patients. Elective repair was performed after angiography in the group presenting late without ischaemia. At operation popliteal artery contusion with local thrombosis was present in all 12 patients who sustained blunt trauma. Penetrating trauma resulted in popliteal artery transection (3), laceration (5), arteriovenous fistula (5) and false aneurysm (3). A medial approach was used in 27 patients and a posterior approach in one patient. Arterial repair utilized reversed autogenous vein in 12 patients; prosthetic grafts (GORE-TEX* 3, velour 1) were used in 4 patients who had no suitable autogenous vein (*Table 3*). Segmental resection and primary end-to-end repair was performed in nine patients. Single patients had a vein patch and lateral arterial repair, respectively. One patient required primary arterial ligation and amputation for irreversible ischaemia. Venous injury was repaired by vein graft (3), lateral suture (6) and end-to-end repair (2) in 11 patients. One patient had popliteal vein ligation.

Fasciotomy as an adjunct to arterial repair was performed in 12 patients during the initial procedure; four-compartment two-incision decompression was used in eight patients and anterior compartment decompression in four patients. One patient had a delayed fasciotomy 8 h following arterial repair. Regional distal heparinization after vascular control was used in all ischaemic limbs. No patient received systemic or postoperative anticoagulation. Distal Fogarty balloon thrombectomy was used routinely before completion of the vascular repair. All patients received intravenous cephalosporin for 24 h. Antibiotic therapy was extended in soft tissue damage or reinstituted when indicated by local or nosocomial sepsis. Soft tissue debridement and orthopaedic fixation generally followed vascular repair. Three patients with limb ischaemia and gross joint and bony instability required temporary silastic arterial shunting to allow fracture stabilization before definitive arterial repair. Delayed skin cover with split skin grafting was necessary in 10 patients. No patient had primary peripheral nerve repair performed.

Results

There was no operative or late mortality. Three (10·7 per cent) patients required limb amputation following blunt injury. One patient had extensive soft tissue trauma with a posterior dislocation of the knee after a crush injury at sea. A 2 day delay before treatment resulted in irreversible ischaemia and required

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Table 1 *Clinical presentation in popliteal artery trauma*

Distal ischaemia	18
Popliteal haematoma	18
False aneurysm	4
Arteriovenous fistula	5
Arterial bleeding	4
Distal emboli	1
Proximity injury	3
Diminished sensation	9
Multiple signs ($\geqslant 2$)	20

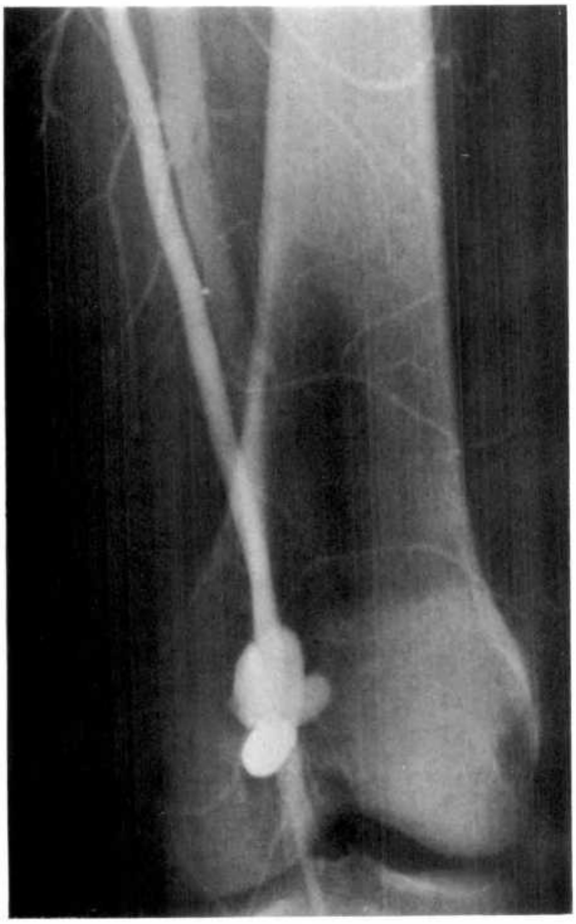

Figure 1 *Femoral arteriogram illustrating a popliteal false aneurysm undetected clinically*

primary ablation. Two patients had unsalvageable distal orthopaedic and degloving injuries with muscle necrosis and progressive sepsis uncontrolled by repeated debridement and had amputations despite having patent vascular repairs. Early failure of the arterial repair occurred in two patients following segmental resection with end-to-end anastomosis after blunt trauma and required revision with interposition vein grafting. A third patient developed claudication secondary to late popliteal arterial occlusion 17 months after resection with end-to-end repair of a popliteal arteriovenous fistula and required a saphenous interposition vein graft. The latter graft occluded 8 h after surgery due to a distal anastomotic intimal flap and is patent 2 years after revision.

Prolonged leg oedema occurred in three patients with associated venous injuries. One patient had primary venous ligation and two patients had ankle swelling following lateral repair of multiple popliteal venous lacerations due to shotgun injuries. Venography and impedance plethysmography in the latter two patients showed patent but narrowed vessels. Five patients with peripheral nerve injuries have residual functional impairment and required prolonged physiotherapy and rehabilitation. Three patients had long-term orthopaedic sequelae with limb instability or joint flexion deformities. The duration of hospital stay ranged from 1 to 13 weeks with a mean of 5·7 weeks in the blunt trauma group and 1·9 weeks in patients with penetrating injuries. The median follow-up in this series is 34 months, ranging from 5 to 70 months. Significant functional disability persists in 5 of 12 (42 per cent) patients with blunt trauma.

Discussion

The principles of vascular repair are well established. The standard treatment of popliteal arterial injury by arterial ligation during World War II resulted in a prohibitively high limb loss of 73 per cent[2]. The introduction of primary arterial repair techniques and rapid evacuation of casualties during the Korean and Vietnam Wars reduced amputation rates to 32 per cent[3,4]. Recent publications of civilian arterial trauma have documented further improved limb salvage[1,5].

Early recognition of arterial injury is essential for effective management. Penetrating or orthopaedic trauma in close proximity to the knee requires careful evaluation for potential vascular injury. The importance of a popliteal haematoma has been emphasized as an early diagnostic sign[6,7] while an enlarging or expansile haematoma is pathognomonic of an

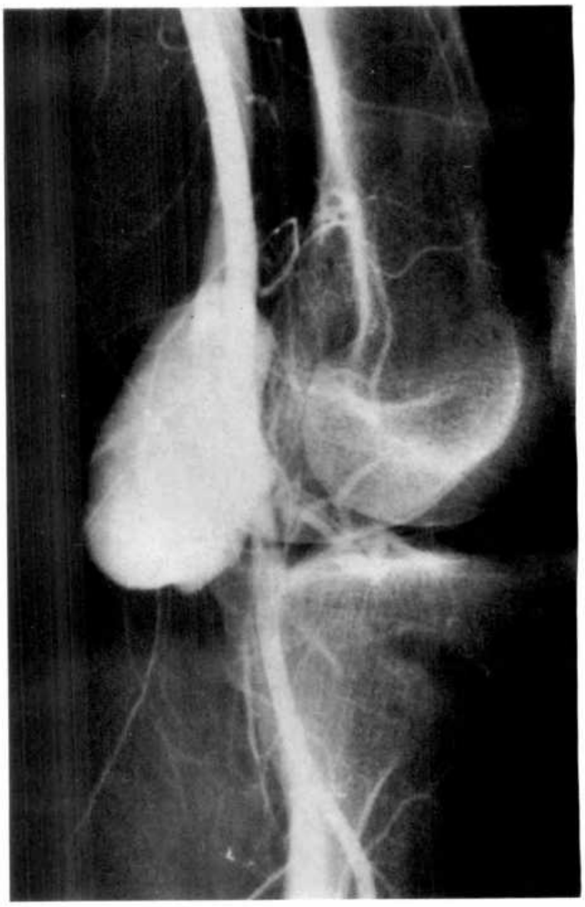

Figure 2 *Angiogram showing an asymptomatic popliteal false aneurysm presenting with digital emboli*

Table 2 *Local injury associated with popliteal artery trauma*

	n	%	Penetrating injury	Blunt trauma
Vein	12	42	12	0
Nerve	6	21	5	1
Bone and joint	12	42	2	10
Soft tissue	14	50	5	9

Table 3 *Arterial repair in popliteal artery trauma* (n = 28)

Vein graft	
Saphenous	11
Cephalic	1
End-to-end repair	9
Synthetic graft	4
Vein patch	1
Lateral repair	1
Ligation	1

arterial injury[8]. The diagnosis is usually clinically apparent. The classical features of acute limb ischaemia are obvious, while arterial bleeding, a bruit or thrill are further reliable indicators of arterial injury. Using these criteria, 24 (85 per cent) patients in the present series had an accurate diagnosis made by careful clinical assessment alone. In the presence of hypotension or extremity oedema we have found Doppler flow studies useful in the initial assessment of pedal pulses to confirm the diagnosis of acute arterial interruption. The presence of a palpable distal pulse however, does not exclude an arterial injury[9,10] and delayed thrombotic occlusion secondary to intimal dissection after knee dislocation is well documented[6,11]. In our series pedal pulses were palpable in eight (29 per cent) patients with either popliteal false aneurysms or arteriovenous fistulae.

The role of angiography in vascular trauma is undisputed. We believe that routine pre-operative angiography is unnecessary in localized popliteal arterial injury, while delay may be detrimental in the critically ischaemic limb. We have favoured the selective use of angiography in multilevel skeletal injury, multiple penetrating wounds, extensive blunt soft tissue injury and orthopaedic trauma with equivocal signs. Arteriography may, in addition, aid surgical strategy with arteriovenous fistulae and reconstruction in the elderly atherosclerotic patient. We regard careful biplanar angiography as essential in delineating small or multiple arteriovenous fistulae (*Figure 3*). Single exposure angiography in the operating theatre reduces treatment delay and the risk of transferring critically injured patients to the radiology department[5,12]. The value of intra-operative angiography in assessing anastomotic patency and the adequacy of distal outflow has been emphasized[13].

The ischaemic period is the critical factor determining limb survival[14]. Correlation of the ischaemic period with ultimate limb viability demonstrated striated muscle tolerance to be approximately 6 h for complete ischaemia[15]. An ischaemic interval >8 h led to an 89 per cent amputation rate[14] while the Vietnam experience reported no limb salvage with total ischaemic periods >12 h[16]. In the experimental situation, equivalent injuries in animal studies have emphasized the critical period following popliteal occlusion[17]. In the clinical context however, relative degrees of ischaemia exist and no absolute interval precludes vascular repair[18]. Successful revascularization has been documented after 36 h[19], 72 h and 4 days[20] following popliteal arterial disruption or occlusion with knee dislocation. The eventual functional result is dependent on arterial perfusion, collateral circulation, extent of soft tissue injury and the presence of hypotension[6]. The development of small vessel thrombosis is the limiting factor influencing satisfactory outcome[21]. Successful limb salvage was achieved 7, 8, 15 and 48 h after popliteal occlusion in our series and stresses the individual variability in the results of delayed revascularization.

The mechanism of injury dictates the method of repair. The classic procedure in popliteal arterial injury is excision of the damaged segment with reversed saphenous vein grafting. Since high velocity wounds and blunt trauma may involve extensive intimal damage, resection of the injured vessels must be adequate. Defects >1·5 cm seldom allow tension-free primary repair without excessive mobilization and sacrifice of genicular collaterals. Direct end-to-end repair is not recommended in blunt trauma. Two cases in this series with arterial resection and primary repair following blunt trauma resulted in early postoperative thrombosis, requiring revision and vein grafting with satisfactory outcome. Two of our patients with minimal intimal disruption were repaired by lateral suture or vein patching, but this technique should be used with caution in the popliteal artery where quality of repair is crucial; any narrowing at the repair site demands resection and conventional repair. In the trauma situation, the graft of choice is autogenous vein. The hazards of sepsis and secondary graft thrombosis in combat casualties have generally precluded the use of synthetic material[22]. Recent studies indicate successful results with synthetic grafts after vascular injury with patency rates equal to those of autogenous saphenous vein grafts in the short length replacements generally required in traumatic vascular wounds[23,24]. Four patients with closed injuries in this series without suitable autogenous vein had synthetic grafting with satisfactory result. None the less, the potential risk of sepsis with penetrating and soft tissue injury makes the routine use of synthetic material undesirable.

Interim intraluminal vascular shunting was used in three patients re-establishing arterial flow rapidly to reduce ischaemic time. This manoeuvre was applied where other severe injuries took precedence over vascular repair and has been used with success in other series[8,15,25]. The use of this technique has also been recommended for venous injuries to reduce venous pressure and distal oedema during arterial repair[25]. Selected use of extra-anatomic bypass grafting from the distal superficial femoral artery to the proximal tibioperoneal trunk has been reported to simplify reconstruction by preserving vital genicular collateral vessels and by limiting dissection[26]. This technique is clearly contra-indicated with arteriovenous fistulae or suspected venous injury and has limited application.

Recognition has been given to the importance of primary venous repair, wherever possible. Venous ligation is followed by 51 per cent incidence of venous hypertension and leg oedema

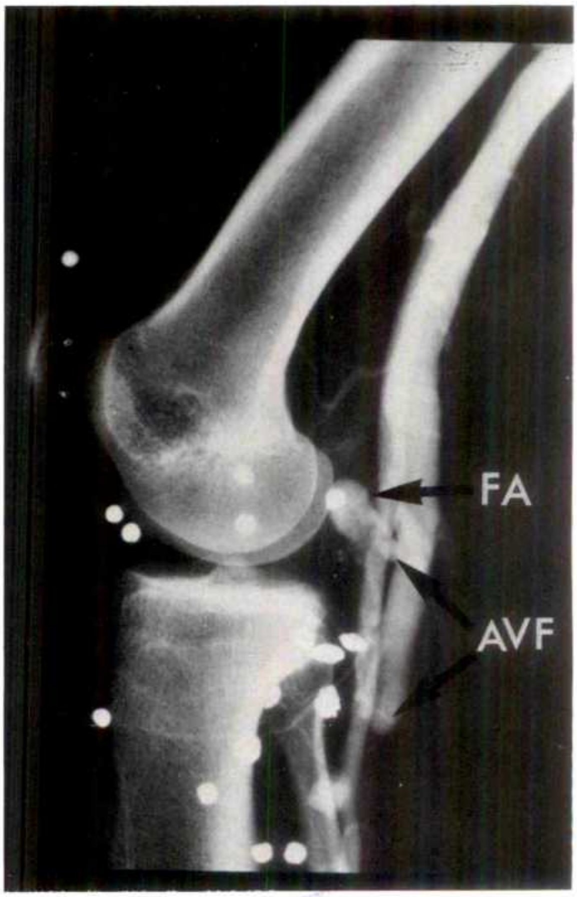

Figure 3 *Lateral view of angiogram demonstrating false aneursym (FA) and arteriovenous fistulae (AVF) not identified on anteroposterior view*

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compared with 13 per cent after repair[27]. We have been able to repair the majority of venous injuries by simple lateral suture. In only 3 of 12 venous repairs were interposition vein grafts necessary. Fasciotomy comprises an important element in limb salvage after popliteal artery injury. We have employed liberal but selective criteria based on clinical assessment using an ischaemic interval >6 h before revascularization, associated venous injury, extensive soft tissue trauma and increased tissue turgor of the calf as indications for early fasciotomy. We believe subcutaneous fasciotomy has a limited role in trauma without permitting adequate decompression and therefore advocate full length fasciotomy incising both skin and fascia.

The frequency of compound fractures, wound contamination and soft tissue injury makes sepsis a significant factor in prolonging postoperative morbidity. Our criterion for adequacy of soft tissue debridement has been visible bleeding and we regard repeated meticulous excision of contaminated or questionably viable tissue as mandatory. The management of associated fractures by either internal or external fixation remains unresolved. Our standard approach in contaminated wounds and blunt trauma has been exoskeleton fixation or skeletal traction, followed, when necessary, by delayed internal fixation. This method reduces operating time, diminishes further compromise of the collateral circulation and is recommended for speed, simplicity and low sepsis rate.

References

1. Snyder WH. Vascular injuries near the knee: an updated series and overview of the problem. *Surgery* 1982; **91**: 502–6.
2. De Bakey ME, Simeone FA. Battle injuries of the arteries in World War II: an analysis of 2471 cases. *Ann Surg* 1946; **123**: 534–79.
3. Hughes CW. Arterial repair during the Korean War. *Ann Surg* 1958; **147**: 555–61.
4. Rich NM, Baugh JH, Hughes CW. Popliteal artery injuries in Vietnam. *Am J Surg* 1969; **118**: 531–4.
5. Lim LT, Michuda MMS, Flanigan DP, Pankovich A. Popliteal artery trauma. *Arch Surg* 1980; **115**: 1307–13.
6. Lefrak EA. Knee dislocation. *Arch Surg* 1976; **111**: 1021–4.
7. Mufti MA, La Guerre JN, Potraczevsky R *et al.* Diagnostic value of hematoma in penetrating arterial wounds of the extremities. *Arch Surg* 1970; **101**: 562–9.
8. Eger M, Golcman L, Schmidt B, Hirsch M. Problems in the management of popliteal artery injuries. *Surg Gynecol Obstet* 1972; **134**: 921–6.
9. Drapanas T, Hewitt RL, Weichart RF *et al.* Civilian vascular injuries: a critical appraisal of three decades of management. *Ann Surg* 1970; **172**: 351–60.
10. Perry MO, Thal ER, Shires GT. The management of arterial injuries. *Ann Surg* 1971; **173**: 403–8.
11. Reckling FW, Peltier LF. Acute knee dislocations and their complications. *J Trauma* 1969; **9**: 181–91.
12. Ransom KJ, Shatney CH, Soderstrom CA, Cowley RA. Management of arterial injuries in blunt trauma of the extremity. *Surg Gynecol Obstet* 1981; **153**: 241–6.
13. Plecha FR, Pories WJ. Intraoperative angiography in the immediate assessment of arterial reconstruction. *Arch Surg* 1972; **105**: 902–7.
14. Green NE, Allen BL. Vascular injuries associated with dislocations of the knee. *J Bone Jt Surg* 1977; **59A**: 236–9.
15. Majeski JA, Gants A. Management of peripheral arterial vascular injuries with a Javid Shunt. *Am J Surg* 1979; **138**: 324–5.
16. Gorman JF. Combat wounds of the popliteal artery. *Ann Surg* 1968; **168**: 974–80.
17. Miller HH, Welch CS. Quantitative studies on the time factor in arterial injuries. *Ann Surg* 1949; **130**: 428–38.
18. Robbs JV, Baker LW. Arterial trauma involving the lower limb. *J Trauma* 1978; **18**: 324–8.
19. Doporto JM, Rafique M. Vascular insufficiency complicating trauma to the lower limb. *J Bone Jt Surg* 1969; **51B**: 680–5.
20. MacGowan W. Acute ischaemia complicating limb trauma. *J Bone Jt Surg* 1968; **50B**: 472–81.
21. Snyder WH, Watkins WL, Whiddon LL, Bone GE. Civilian popliteal artery trauma: an eleven year experience with 83 injuries. *Surgery* 1979; **85**: 101–8.
22. Rich NM, Hughes CW. The fate of prosthetic material used to repair vascular injuries in contaminated wounds. *J Trauma* 1972; **12**: 459–67.
23. Lau JM, Mattox KL, Beall AC *et al.* Use of substitute conduits in traumatic vascular injury. *J Trauma* 1977; **17**: 541–6.
24. Shah DM, Leather RP, Corson JD *et al.* Polytetrafluoroethylene grafts in the rapid reconstruction of acute contaminated vascular injuries. *Am J Surg* 1984; **148**: 229–39.
25. Barros D'Sa AAB. A decade of missile-induced vascular trauma. *Ann R Coll Surg Engl* 1982; **64**: 38–44.
26. Daugherty ME, Sachatello CR, Ernst CB. Improved treatment of popliteal arterial injuries. *Arch Surg* 1978; **113**: 1317–21.
27. Rich NM, Hobson RW, Collins GJ, Andersen CA. The effect of acute popliteal venous interruption. *Ann Surg* 1976; **183**: 365–8.

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Staphylococcal infection of open granulating wounds

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The significance of staphylococcal infection has been studied prospectively in 250 wounds healing by open granulation. In a series of 50 axillary skin excisions, 17 became infected with Staphylococcus aureus *with consequent pain and delay in healing. The infections responded well to Fucidin ointment. Nasal carriers of the organism may be especially liable to this complication. In contrast, although* S. aureus *was not infrequently found in deep granulating wounds, there was no clear evidence of harm resulting in the 50 laparotomy wounds and 150 pilonidal sinus excisions studied. The susceptibility of superficial wounds to the infection is ascribed to friction from dressings. Deep granulating wounds are occasionally affected similarly when the cavity has filled.*

Keywords: Granulating wounds, staphylococcal infection, wound infection, wound healing rate

The susceptibility of fresh surgical wounds to serious infection by *Staphylococcus aureus* is well known[1]. In contrast, open granulating wounds are generally considered to be resistant to outside infection. In the present study of 200 deep wounds healing by open granulation (50 laparotomy wounds and 150 pilonidal sinus excisions) this presumption appeared to be justifiable. However, this was not the case with the superficial wounds studied, namely 50 excisions of axillary skin for suppurative hidradenitis. The character of staphylococcal infection of such wounds is described and the value of prompt specific treatment is illustrated.

Statistical methods have been described previously for predicting the time taken by healthy laparotomy wounds and pilonidal sinus excisions to heal by open granulation[2,3]. A formula of the same type has been determined here for excisions of axillary skin.

Methods

Selection of patients: wound care

The three groups described above each consisted of consecutive patients attending a clinic for open granulating wounds in the University Hospital of Wales who were followed either until their wounds healed or until they were referred for surgical revision. All the wounds were dressed in the clinic with Silastic foam, changing to a textile dressing in the later stages of healing as previously described[3]. The mean interval between operation and first attendance at the clinic was 9 days for pilonidal sinus excisions, 14 days for skin excisions and 23 days for laparotomy wounds. Wounds were briefly bathed twice daily using a heaped tablespoonful of salt in a small bath of water. Alternatively, patients could direct a shower on the wound for 10–15 s to flush away loose debris.

Excisions of axillary skin

The first 25 wounds were managed conservatively, i.e. simply by bathing the wound and cleansing the Silastic foam dressing twice daily, a new dressing being made weekly. However, three of the nine wounds infected with *S. aureus* were finally treated with Fucidin ointment on ethical grounds because of considerable delay in healing. The remaining 25 wounds were managed actively, i.e. prompt treatment was given to the eight infected wounds (Fucidin ointment to five, Graneodin to one, silver nitrate soaks to one, while one case needed only modification of the dressing to avoid friction).

Laparotomy wounds

The 50 wounds studied had either been re-opened to heal by granulation because of overt infection or they had been left unsutured as a precaution in high-risk cases. One patient was excluded from the series, a diabetic being treated by diet alone.

Pilonidal sinus excisions

150 patients were studied in whom excision of a pilonidal sinus or abscess had been carried out and the wound left open to heal by granulation. There were 74 emergency operations and 71 planned, while 5 cases lacked a record.

Bacteriology: evidence of infection

Semi-quantitative cultures were made in air and hydrogen as described previously[3]. All wounds were cultured at the first clinic attendance and in the case of the laparotomy wounds subsequently at 1 or 2 week intervals. Otherwise, swabs were only repeated if there was clinical evidence of infection, namely pain or discomfort, tenderness of the wound, a discoloured or inflamed appearance and a seropurulent or blood discharge. Antibiotics were not prescribed in the absence of such clinical evidence.

Swabs for nasal carriage of staphylococci were first moistened with sterile water. They were plated on blood–agar and incubated for 2 days. No pre-operative cultures of axillae were made.

Prediction of healing time: statistical analysis

Healing time was predicted by a formula based on a wound dimension (WD). The WD for laparotomy wounds and pilonidal sinus excisions was either the width or the depth in mm, whichever was greater. The formula established for predicting the healing time of laparotomy wounds is $(\mathrm{WD} \times 1{\cdot}19)+3{\cdot}6$ days (Reference 2) and that for pilonidal sinus excisions is $(\mathrm{WD} \times 1{\cdot}23)+4{\cdot}3$ days (Reference 3). The WD for axillary skin excisions is the width, i.e. the vertical dimension, imagining the arm to be held high, and the predicted time determined by the present study is $(\mathrm{WD} \times 0{\cdot}76)+6{\cdot}7$ days. 'Delay in healing' was calculated by subtracting each predicted healing time from the time actually observed as described in the earlier papers for laparotomy and pilonidal sinus wounds. Six pilonidal sinus excisions referred for re-operation were assigned an arbitrary delay of 110 days (*Figure 1*). The significance of differences in mean delay was assessed by the t test and the Wilcoxon rank sum test, and other comparisons by Fisher's exact test.

Results

Axillary skin excisions

Of the 50 wounds studied, 17 had clinical and bacteriological evidence of *S. aureus* infection. The relation of the healing time of the 33 healthy excisions to their wound dimension (WD) is shown in *Figure 2*, the formula derived from the regression line to predict normal healing time being $(\mathrm{WD} \times 0{\cdot}76)+6{\cdot}7$ days. *Figure 3* compares the 'delay in healing', i.e. observed time minus predicted time, of the healthy wounds (0 days, $\pm 1{\cdot}93$ (mean $\pm$ s.e.m.)) with the delay for nine staphylococcal infections managed conservatively (mean $42{\cdot}0 \pm 6{\cdot}12$) and eight treated promptly as described above (mean $15{\cdot}5 \pm 4{\cdot}46$). The interference to healing by staphylococcal infection was highly significant in both series ($P < 0{\cdot}01$) but so was the advantage of prompt treatment over conservative management.

Figure 4 illustrates a staphylococcal infection of the lower part of an axillary skin excision. The clinical features are detailed in the Discussion section. Fucidin ointment relieved the symptoms immediately and progress towards healing resumed.

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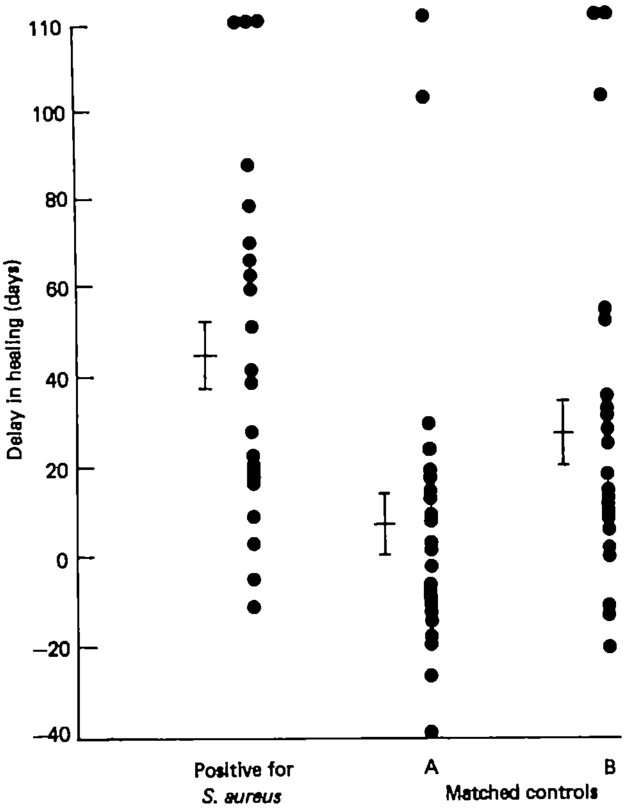

Figure 1 *The healing of pilonidal sinus excisions yielding* S. aureus *compared with that of (A) cases matched for age, sex, wound dimension and emergency or planned operation and (B) cases matched also for the occurrence of anaerobic bacteria. There is a significant difference in the case of A but not B (mean ± s.e.m. shown). Cases referred for re-operation were assigned an arbitrary delay of 110 days*

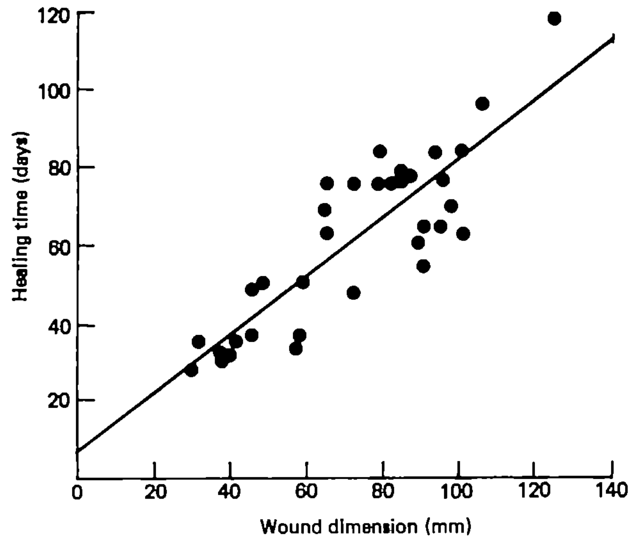

Figure 2 *The relation of healing time to wound dimension (width) in 33 healthy excisions of axillary skin healing by open granulation. Slope, 0·76; intercept, 6·7; r = 0·85*

Laparotomy wounds

S. aureus was isolated from 9 of the 50 wounds studied and anaerobic bacteria persistently from 7. As the analysis presented in *Figure 5* shows, the latter were associated with delay in healing but *S. aureus* on its own was not. Anaerobic infection appeared to favour colonization of wounds with staphylococci, the degree of coincidence being significant ($P = 0·027$). However, the mean delay of 60·7 days (s.e.m. ±24·58) seen with this association did not differ significantly from that of 47·7 days (s.e.m. ±28·43) seen with anaerobes alone ($P = 0·35$).

Pilonidal sinus excisions

S. aureus was isolated from 23 wounds, the mean delay in healing being 45·7 days (s.e.m. ±7·68). A series taken from the remaining 127 wounds to match these for age, sex, wound dimension and planned or emergency operation had a mean delay of 7·6 days (s.e.m. ±7·39), a highly significant difference ($P < 0·01$). However, as shown in *Figure 1* in a series with the matching extended to include a similar occurrence of anaerobic bacteria in the wound flora, the mean delay became 27·1 days (s.e.m. ±7·65) and the difference from the staphylococcal group was no longer significant ($P = 0·09$). It appeared therefore that the adverse connotation of *S. aureus* isolations was largely, or possibly wholly, due to their association with anaerobes. Anaerobic bacteria were isolated from 21 of the 23 excisions positive for *S. aureus* but from only 57 of the other 127 wounds, the apparent dependence of staphylococci on their presence being highly significant ($P < 0·01$).

Discussion

The concern of the present study is the patient discharged from hospital with an open granulating wound to be cared for at home. The majority of such wounds are healthy, free from significant bacteria and resistant to infection from external sources if properly managed. Indeed, if they are painless and have a normal appearance it is unwise to examine them bacteriologically because transient organisms may lodge accidentally and harmlessly on the surface and their presence be

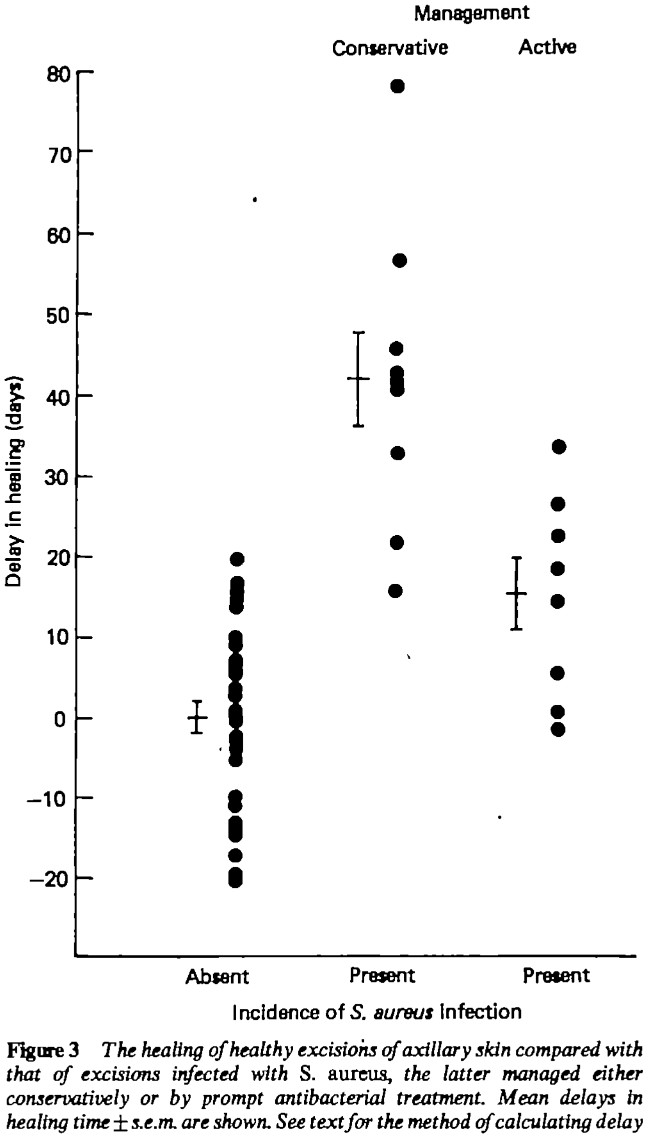

Figure 3 *The healing of healthy excisions of axillary skin compared with that of excisions infected with* S. aureus, *the latter managed either conservatively or by prompt antibacterial treatment. Mean delays in healing time ± s.e.m. are shown. See text for the method of calculating delay in healing*

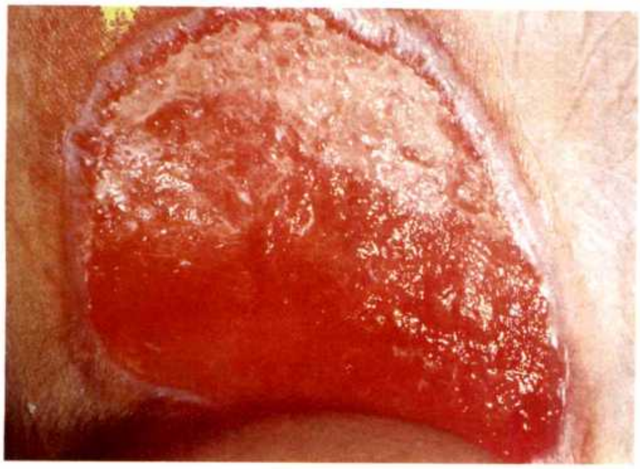

Figure 4 *Infection of the lower part of an axillary skin excision with* S. aureus. *The normal fibrinous surface membrane seen in the upper part of the wound has been lost in the affected area*

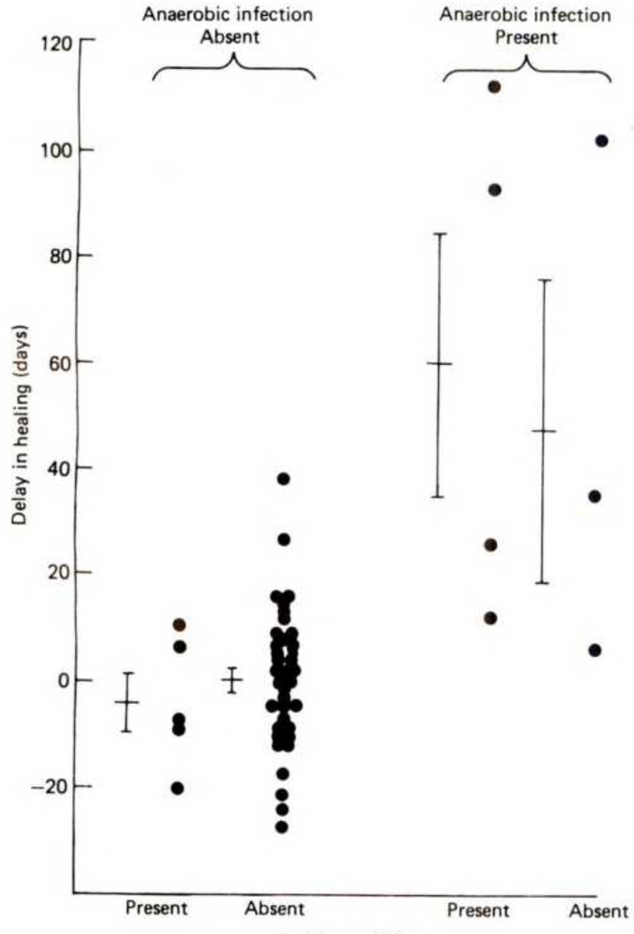

Figure 5 *The significance of* S. aureus *isolation in relation to anaerobic infection in 50 laparotomy wounds healing by open granulation. There was no delay in healing in the absence of anaerobic infection and staphylococci had no obvious significance in its presence (means ± s.e.m. shown)*

misunderstood. However, some open granulating wounds remain infected or become clinically infected and when *S. aureus* is isolated from these the problem of assessing its significance arises. Early studies of postoperative sepsis attached prime importance to the organism, although even then it was recognized that it could be isolated also from healthy wounds[4,5]. Unfortunately, this work suffered from a failure to detect the key role of anaerobic bacteria in wound infection. Parker has pointed out that most burns become infected with *S. aureus* but that this need not delay healing or prevent grafts from taking[6]. Decubitus ulcers are often temporarily colonized by the organism and even when it is persistent the rate of healing appears to be unaffected[7].

In our two series of laparotomy wounds and pilonidal sinus excisions, *S. aureus* appeared at first sight to make an important contribution to wound infection. However, further analysis using delay in healing as the index showed that its apparent significance was largely or wholly due to an association with anaerobic infection. Our conclusion is that the tissue damage resulting from anaerobic infection encourages colonization by staphylococci but that such superinfection is of little or no importance. Indeed, if *S. aureus* is isolated from an infected deep granulating wound an underlying anaerobic infection should be suspected. The significance of such infection has been described previously[2,3].

In contrast to its relative unimportance when isolated from deep granulating wounds, *S. aureus* was responsible for pain and delayed healing in about a third of our series of axillary skin excisions. Such infection can be recognized clinically, the wound being painful and tender on pressure, inflamed and wet with sero-purulent exudate while fibrinous membrane initially present on the surface tends to dissolve away (*Figure 4*). Healing stops and the wound may even enlarge owing to splits in recent scar tissue. Semi-quantitative culture gives a swab count of 10^4 colonies or more of *S. aureus*. Fucidin ointment quickly controls the infection but its use may be disallowed in hospitals to reduce the risk of generating drug-resistance. Topical gramicidin or bacitracin can be used for inpatients, although these appear to be less reliable. Mild infection can be treated with soaks of 0·5 per cent silver nitrate, reducing to 0·25 per cent after some days. Topical treatment was chosen because of the superficial nature of the infection.

Deep granulating wounds eventually become superficial and occasionally staphylococcal infection then supervenes to prevent healing. As in the case of axillary skin excisions, we suspect that the predisposing cause is friction from dressings, which may be inevitable owing to body movement. The rubbing presumably damages the surface layer of tissue, making it susceptible to infection by external staphylococci. We have occasionally noted fine bleeding points on wound surfaces subjected to friction. Dressings should be designed to reduce friction to the minimum.

In a study in progress, the six patients with infected axillary excisions so far met were all nasal carriers of *S. aureus* on first attendance at the wound clinic. The elimination of such carriage is worth consideration with this type of operation.

References

1. Lidwell OM. Some aspects of the transfer and acquisition of *Staphylococcus aureus* in hospitals. In: Macdonald A, Smith G, eds. *The Staphylococci.* Aberdeen: Aberdeen University Press, 1981: 175–202.
2. Marks J, Hughes LE, Harding KG, Campbell H, Ribeiro CD. Prediction of healing time as an aid to the management of open granulating wounds. *World J Surg* 1983; 7: 641–5.
3. Marks J, Harding KG, Hughes LE, Ribeiro CD. Pilonidal sinus excision – healing by open granulation. *Br J Surg* 1985; **72**: 637–40.
4. Report by the Public Health Laboratory Service. Incidence of surgical wound infection in England and Wales. *Lancet* 1960; **ii**: 659–63.
5. Report by the Committee on Trauma, National Academy of Sciences, Chairman Howard JM. Postoperative wound infections. *Ann Surg* 1964; Suppl 2.
6. Parker MT. Staphylococcal diseases. IN: Smith GR, ed. *Topley and Wilson's Principles of Bacteriology, Virology and Immunity*. 7th ed. Vol 3. *Bacterial diseases.* London: Edward Arnold, 1984: 257.
7. Daltrey DC, Rhodes B, Chattwood JG. Investigation into the microbial flora of healing and non-healing decubitus ulcers. *J Clin Pathol* 1981; **34**: 701–5.

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Auditing the vascular surgical audit

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The results are presented of vascular surgical audits in Oxford over the 10 years 1975–85. Changes observed include the decreasing use of endarterectomy (other than carotid); the introduction of transluminal angioplasty, and fewer lumbar sympathectomies. The number of major amputations has increased relative to arterial reconstructions. Our audit methods over the 10 years included the use of punch cards, two different computer programs, and a simple weekly audit of cases. The relative merits of these methods are compared. Numbers of procedures performed in Oxford were compared with expected figures calculated from the Hospital In-patient Enquiry, the Lothian audit, and the Vascular Surgical Society survey. In general the calculated and actual numbers are similar. Difficulties in finding comparable operation categories and the totally inadequate classification of nationally collected data highlight the need for improved audit in vascular surgery.

Keywords: Amputation, aneurysm, arterial occlusive diseases, computers, vascular diseases

Planning of manpower and training requirements in any surgical discipline demands accurate information on actual and projected workloads. Some information is available from DHSS figures[1,2], from the Hospital In-patient Enquiry[3], and from published local audits[4–9], but only one[9] addresses the changing pattern of vascular surgical workload. Most district general hospitals now employ at least one surgeon with a special interest in vascular surgery. The number of referrals and operative procedures in any community will determine the number of vascular surgeons needed and the extent of their commitment to vascular work. An attempt to obtain information on the numbers of vascular operations performed has been made by the Vascular Surgical Society of Great Britain and Ireland, which has recently conducted a survey in three regions[10].

Surgical units with an interest in audit have used various methods of collecting data[4–9] and computers have become popular because of their capacity for storage and rapid collation of data. Computerized audit requires careful planning, and reliable input of information by skilled personnel. Simple written methods may still be appropriate especially when complicated manipulation of data is not needed.

We report the results of 10 years' audit of vascular surgical practice in Oxford. Different methods of data collection were used during this period, including punch cards, written records and computers. We present the results of this audit, with comments on the merits of the various methods used, and comparisons between our experience and available information from the rest of the United Kingdom.

Material and methods

The Vascular Surgical Unit

The Vascular Surgical Unit at the John Radcliffe Hospital currently serves a local community of 522 000 in the Oxford Health District and also receives some referrals from further afield. The unit deals with all emergency and elective vascular cases both at a specialist vascular clinic and on admission to the hospital. This service is provided at present by three consultants (who also have commitments to general surgery and transplantation), one lecturer (senior registrar), and two house surgeons (also dealing with general surgery). During the early years of the audit the service was provided by two consultants, one lecturer (senior registrar) and two house surgeons.

Method of audit

Details of all vascular surgical procedures performed between 1975 and 1985 were recorded by the following methods.

Computer. A computer database system was developed and programmed by a member of the clinical staff (I.G.K.) on the Oxford University ICL 2980 computer. The first full year of data collection by the computer was 1 January 1980 to 31 December 1980, and its use continued until the end of October 1983 when, because of dissatisfaction with the system, it was no longer used for recording operation details, which form the basis of this report. It has also been used to record details of new patients, arteriograms and follow-up. New patient data are still entered on to this system.

From 1 November 1983 to 31 October 1984 details were transferred from weekly mortality and morbidity reports (see below) to a new simple database 'package' on the university computer.

Punch cards. The earliest prospective audit of vascular surgery in Oxford was by punch cards, and details were collected in this way for the two years 1 August 1977 to 31 July 1978 and 1 January 1979 to 31 December 1979.

Later, a second prospective one-year punch card audit was kept by one vascular lecturer (R.G.S.) during his period of appointment (1 November 1982 to 31 October 1983) in order to assess accurately the experience gained in a year and also to compare with the data retrieved from the ICL 2980 computer program during this period.

Written records. In recent years details have been presented on all patients to a weekly mortality and morbidity meeting, and these are kept as part of a complete written record of the work of the Nuffield Department of Surgery. In addition to mortality and morbidity details they include the name, age and number of every patient admitted to the department, together with diagnoses and details of operations performed. These have been used to produce annual audits of the vascular work for the periods 1 November 1983 to 31 October 1984 and 1 November 1984 to 31 October 1985. For the first of these two years information was entered on to an individually designed computer database program, and for both years numbers of operations were also obtained directly from the written records.

These recent one-year periods each began on 1 November to coincide with the date of rotation of the lecturers/senior registrars on to the unit.

Review of operating theatre ledgers. For the calendar years 1975 and 1976 the numbers of operations were obtained by review of operating theatre ledgers.

Comparison with national figures

Expected numbers of procedures for a population the size of Oxford were computed from the Hospital Inpatient Enquiry (HIPE) for 1983[3], from the recent audit of the Lothian Region[9] and from the Vascular Surgical Society (VSS) survey[10]. The Oxford district population in 1983 was 517 000.

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Table 1 *Total number of operations recorded by the different audit methods during the period 1975–85*

	1975	1976	1977–8	1979	1980	1981	1982	1982–3	1983–4	1984–5
Grafts										
Aorto-ilio-femoral	44	56	57	50	40	53	40	68	60	50
Axillofemoral	—	1	3	8	4	8	7	7	5	6
Femorofemoral	1	1	4	2	2	4	2	5	7	5
Femorodistal	38	61	55	49	35	32	28	41	46	27
Other	15	9	6	8	19	23	38	15	6	3
Endarterectomy										
Carotid	6	3	13	21	14	19	19	20	14	25
Other	23	29	44	23	17	18	16	7	11	4
Profundaplasty	7	2	8	15	—	—	—	0	6	2
Transluminal angioplasty	—	—	0	0	0	0	0	9	15	30
Thrombo-embolectomy	32	43	41	35	43	38	53	38	54	55
Sympathectomy										
Lumbar operative	18	11	17	10	12	8	9	1	7	6
Lumbar phenol	5	20	28	16	58	52	33	35	10	30
Upper thoracic	6	4	4	2	11	—	—	6	4	1
Amputation										
Above knee	20	22	9	10	27	23	17	19	21	16
Gritti-Stokes	2	6	9	12	9	4	19	32	19	28
Through knee	3	—	0	0	1	1	1	0	12	1
Below knee	12	17	15	23	15	33	21	22	21	30
Revision	3	3	2	2	—	—	—	—	9	4
Minor	45	38	48	51	46	37	35	45	38	29
Cervical rib/thoracic outlet	5	2	3	9	9	2	2	5	7	2
Miscellaneous	54	42	12	50	43	130	110	27	26	74
Total	339	370	378	396	405	485	450	402	398	428

Results

General trends (Table 1)

Striking changes during the 10 years were the decreasing use of endarterectomy (other than carotid) and the introduction of transluminal angioplasty. There was a trend towards fewer lumbar sympathectomies over the years, but the overall numbers of lumbar sympathectomies varied, probably with the enthusiasm for this procedure of those involved during each year.

There was no discernable trend in the total numbers of arterial reconstructions, while in contrast the number of major amputations increased progressively and doubled in 10 years (*Figure 1*).

The total number of operations performed has shown no general increase. The two years with totals rather higher than the median of 400 show particularly large numbers of procedures classified as 'miscellaneous' and retrieved in this group from the computer.

Comparison of punch cards and computer records

The punch card system kept by the vascular lecturer between 1 November 1982 and 31 October 1983 showed good, but not exact, correlation with the computer totals for the same period. The main defect of the computer system was in classification. For example, 112 arterial grafting procedures were recorded on the punch cards, compared with 110 retrieved by the computer, but there was a discrepancy of 28 in details of classification, accounted for largely by the computer 'miscellaneous' category.

Comparison with national figures

Direct comparisons were difficult because the different surveys and reports did not present uniform categories of operations. *Table 2* shows similar groups of procedures, comparing the numbers performed in Oxford with the numbers expected from the HIPE[3], Lothian[9] and VSS survey[10] figures.

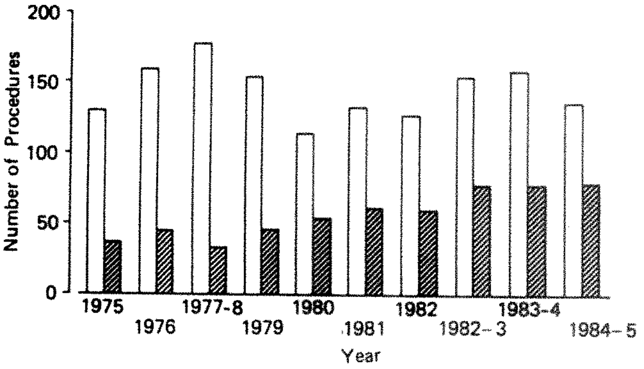

Figure 1 *Histogram showing the numbers of arterial reconstructions,* ☐, *and major amputations,* ▨, *each year during the period 1975–85*

Discussion

Most of the changes observed in our practice over the period of this review have followed generally recognized trends in vascular surgery. The decreasing use of endarterectomy at sites other than the carotid, and the introduction of transluminal angioplasty are the most important of these. The increased number of amputations compared with reconstructions is accounted for in part by the rising age of the population served but is otherwise difficult to explain[11].

It is interesting to see that the numbers of operations performed in Oxford in 1983 were similar to the expected numbers calculated from other sources, except in two particular instances. The first discrepancy was the small number of procedures for ruptured aortic aneurysms compared with the number expected from the VSS survey[10]. The ruptured aneurysm incidence in the Lothian report[9] is almost equally small, and review of publications from other centres[12–14] suggests that the VSS survey figure is an overestimate.

The second difference from expected figures was the greater number of carotid endarterectomies performed in Oxford

Table 2 *Numbers of operations performed in Oxford in 1983 (1.11.82–31.10.83) compared with the numbers expected for a population the size of the Oxford district, computed from HIPE for 1983*[3]*, the Lothian audit for 1983*[9]*, and the VSS survey*[10]*. Note that direct comparisons were only possible for a limited number of categories of operation*

	Oxford	Expected from Lothian	Expected from HIPE	Expected from VSS survey
Total arterial grafts	136	143	—	—
Elective aortodistal bypasses	53	—	—	41–62
Emergency/ruptured aortic aneurysm	15	21	—	41–62
Total lower limb amputations	118	131	—	—
Major lower limb amputations	73	—	—	41–83
Amputation through the thigh	51	—	35	—
Amputation through the lower leg (or below knee)	22	—	24	—
Carotid endarterectomy	20	—	see below	10–20
Endarterectomy (total)	27	—	7	—
Operations on arteries of the neck	—	—	6	—

compared with the number expected from the HIPE figures. It is possible that this was due to referral from outside the health district as a result of the special interest of the Oxford unit in carotid disease.

Our experience with different methods of audit has revealed problems peculiar to each. Punch cards work well for a time but become unmanageable for periods longer than about a year. In contrast we found that for a single year it was not worth using a computer system to perform a simple audit. The computer program employed in 1983–4 was rapid and simple to use, but when results were cross-checked with our mortality and morbidity records at the end of the year, it was found that detailed totals could be obtained by hand from these within 2 or 3 h – a much shorter time than that expended on the computer during the year.

The dedicated computer program used from 1980 to 1983 was subject to several problems, related as much to personnel as to the computer itself. In summary these problems and the lessons learnt from them were:

1. The vascular nurse responsible for entering data was not in a post permitting locum cover, and during her absence caused by pregnancy there was a considerable backlog and loss of some data. It is important to have one person responsible for collating and entering all data with definite arrangements for a locum if they are absent for any length of time. A single coordinator can also be sure that details have been obtained for all patients managed by the unit, and can discipline clinicians to complete forms properly.
2. The program was tedious to use, with slow access. Our computer was programmed in 1978 and operating speeds were considerably slower than today. Consequently it was inefficient to insert data until a sufficient quantity had accumulated to justify the time and effort involved. Quick access to the program and rapid simple use are essential.
3. In retrospect the amount of data we tried to record was too great. Deciding what data to record is difficult and a trial period of audit would be worthwhile before embarking on a long-term project unamenable to change.
4. Clinicians are bad at filling in forms particularly when this task is additional to writing clinical notes or letters to general practitioners. Ideally, recording data for the computer should be a routine part of patient management, the computer data sheet being an integral part of the patient's notes.
5. It was not always possible to retrieve data in the required form. The clinician who programmed the computer could overcome these problems, but when he left Oxford delay was inevitable. It is particularly important to have continuing close contact with a professional computer programmer. The changing environment in a mainframe computer demands frequent updating of the program, while data handling and retrieval require expert help.

Vascular surgical audit at a national level has not kept pace with developments in vascular surgical practice. The HIPE codings are totally inadequate and must be improved if useful information is to be obtained. No attempt has been made in the United Kingdom to keep a large scale vascular registry similar to that of Karmody and colleagues in the United States[15]. We hope that this report of our experience will help those planning audit systems of their own, and encourage publication of their findings as a source of reference for planning vascular surgical services and careers.

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References

1. Fowkes FGR, Page SM, Phillips-Miles D. Surgical manpower, beds and output in the NHS: 1967–1977. *Br J Surg* 1983; **70**: 114–16.
2. Allen-Mersh TG, Earlam RJ. General surgical workload in England and Wales. *Br Med J* 1983; **287**: 1115–18.
3. Department of Health and Social Security and Office of Population Censuses and Surveys. *Hospital Inpatient Enquiry 1983*. London: HMSO, 1985.
4. Gough MH, Kettlewell MGW, Marks CG, Holmes SJK, Holderness J. Audit: an annual assessment of the work and performance of a surgical firm in a regional teaching hospital. *Br Med J* 1980; **281**: 913–18.
5. Gilmore OJA, Griffiths NJ, Connolly JC, Dunlop AW, Hart S, Thompson JPS, Todd IP. Surgical audit: comparison of the workload and results of two hospitals in the same district. *Br Med J* 1980; **281**: 1050–2.
6. Stower MJ, Hardcastle JD, Bourke JB. Surgical emergencies and manpower. *Ann R Coll Surg Engl* 1984; **66**: 117–19.
7. Quill DS, Devlin HB, Plant JA, Denham KR, McNay RA, Morris D. Surgical operation rates: a twelve-year experience in Stockton-on-Tees. *Ann R Coll Surg Engl* 1983; **65**: 248–53.
8. Prout WG, Blood PA. The establishment of a microcomputer-based diagnosis and operations index in the Department of Surgery of a district general hospital. *Br J Surg* 1985; **72**: 48–51.
9. Gruer R, Gunn AA, Gordon DS, Ruckley CV. Audit of Surgical audit. *Lancet* 1986; **i**: 23–6.
10. Darke SG, Bell PRF. Rationalisation of future Vascular Service. Communication of the Vascular Advisory Committee. November 1985.
11. Sethia KK, Berry AR, Morrison JD, Collin J, Murie JA, Morris PJ. Changing pattern of lower limb amputation for vascular disease. *Br J Surg* 1986; **73**: 701–3.
12. Butler MJ, Chant ADB, Webster JHH. Ruptured abdominal aortic aneurysms. *Br J Surg* 1978; **65**: 839–41.
13. Makin GS. Changing fashions in the surgery of aortic aneurysms. *Ann R Coll Surg Engl* 1983; **65**: 308–10.
14. Fielding JWL, Black J, Ashton F, Slaney G, Campbell DJ. Diagnosis and management of 528 abdominal aortic aneurysms. *Br Med J* 1981; **283**: 355–9.
15. Karmody AM, Blumerberg RM, Wall CA. Preliminary experience with a large scale vascular registry. *Am J Surg* 1983; **146**: 162–3.

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One hundred patients ten years after parietal cell vagotomy

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One hundred patients with duodenal or pyloric/prepyloric ulcer disease were operated with parietal cell vagotomy (PCV) and followed for a minimum of 10 years. At 6 weeks, 1,5 and 10 years postoperatively gastric secretory tests, haematological work-up and clinical examination or telephone interview were performed. There was no operative mortality and the frequency of postoperative sequelae was minimal. The cumulative ulcer recurrence rate was 18 per cent and another 14 per cent had slight to moderate symptoms of epigastric pain without any signs of ulcer. Upper gastrointestinal endoscopy was used to reveal recurrences but was performed only if the patient had symptoms of recurrence. A rise in basal acid secretion and in pentagastrin-stimulated secretion was observed the first year postoperatively, whereas insulin-stimulated peak acid output increased during the first 5 years. We conclude that PCV has a low rate of per- and postoperative complications and an acceptable recurrence rate. Therefore, it seems that PCV is the method of choice in chronic duodenal ulcer disease.

Keywords: Gastric acid secretion, peptic ulcer, ulcer recurrence, vagotomy

Among surgeons, partial gastric resection and truncal vagotomy with drainage have a long tradition in the treatment of peptic ulcer disease and, although a high postoperative morbidity has been reported[1,2], the ulcer recurrence rate has been low[3]. With the introduction of parietal cell vagotomy (PCV) without drainage[4,5] it seemed that the search for the ideal surgical treatment for peptic ulcer disease was over. PCV had a low operative mortality rate[6] and the postoperative morbidity was close to that of an unoperated non-ulcer population[7]. However, as time has passed most follow-up studies have revealed a fairly high ulcer recurrence rate[8–11], in one study above 20 per cent[12], with a tendency to increase more than 5 years after surgery[8–9]. Therefore, it is appropriate to study the long term results after PCV.

The aim of the present study is to report a 10 year follow-up of the first 100 patients with chronic duodenal or prepyloric/pyloric ulcer disease in the University of Lund PCV study. Postoperative morbidity and mortality as well as acid secretory data are presented.

Patients and methods

The present study is part of a follow-up of 405 patients operated upon with PCV during the years 1971–1980 at the University Hospital in Lund. A detailed description of the whole patient population, short term ulcer recurrence rate and acid secretory data is published elsewhere[13–15]. Diagnosis of the disease was based on history of illness of more than 2 years and was objectively confirmed with pre-operative endoscopy (90 per cent of the patients) or radiographic double-contrast examination that showed either the presence of an ulcer or a deformity of the pyloric, prepyloric region or the duodenal cap. The pre-operative work-up included a pentagastrin test and the postoperative examinations were performed at 6 weeks, 1,5 and 10 years. The follow-up examinations included patient weight and serum values of haemoglobin, vitamin B_{12}, calcium and serum iron. Upper gastrointestinal endoscopy was used to reveal recurrences but was performed only if the patient had symptoms of recurrence. The acid secretory tests used were pentagastrin (6 µg/kg) and insulin (0·1 units/kg). The spontaneous gastric acid secretion was measured in four 15 min periods (basal acid output). The stimulated secretion was followed for eight periods of 15 min each. The peak acid output was calculated from the two highest consecutive samples multiplied by two. In this study, data from 100 patients followed for a minimum of 10 years are included. The first 25 patients operated upon with PCV at our institution were excluded owing to a non-standardized surgical procedure at that time[13]. Dissection of 5–8 cm of the oesophagus was added to the procedure and the following 125 patients consecutively operated upon were selected in order to collect data from 100 individuals. Fifteen patients were untraceable, two were unwilling to attend follow-up and eight patients have died (cardiopulmonary disease, 3; carcinoma of the lung, 1; carcinoma of the prostate, 1; malignant melanoma, 1; aortic aneurysm, 1; and epilepsia, 1). Seventy-five patients were examined at the follow-up clinic and 25 patients were interviewed by telephone. The data are expressed as medians (interquartile, 25–75 per cent range) and non-parametrical methods (Wilcoxon signed rank sum test) were used when appropriate.

Results

One hundred patients operated upon with PCV during the years 1971–1974 are included. The median age at operation was 45 years (range 21–72 years), 75 per cent of the patients were male. In 71 per cent of the patients a duodenal ulcer was found and in 29 per cent a prepyloric or pyloric ulcer was found. A total of 16 surgeons performed the operations. Except for splenectomy in one patient, the per- and postoperative course was uneventful. Sixteen out of seventy-one patients with duodenal ulcer (22·5 per cent) and two out of twenty-nine patients with

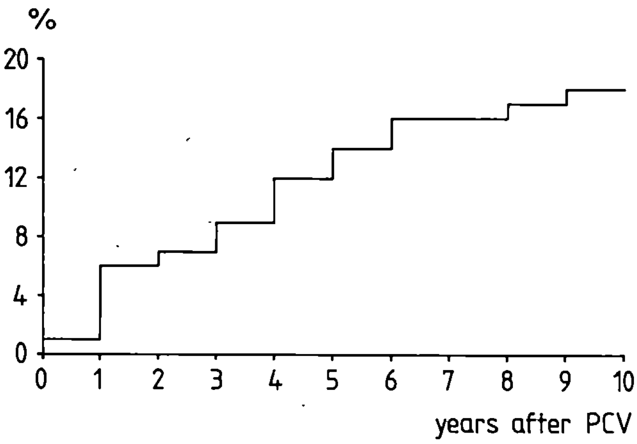

Figure 1 *Cumulative ulcer recurrence rate in 100 duodenal ulcer and prepyloric/pyloric ulcer patients after parietal cell vagotomy*

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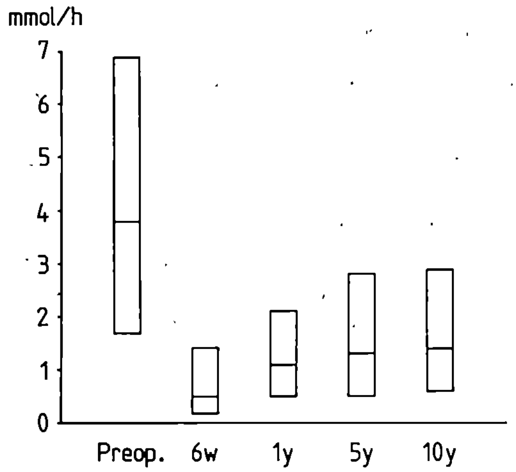

Figure 2 *Basal acid output before and up to 10 years after PCV. Median and interquartile range shown. There is a significant decline between the pre-operative value and the 6 week value* ($P<0.01$) *and a significant increase between the 6 week and 1 year value* ($P<0.01$)

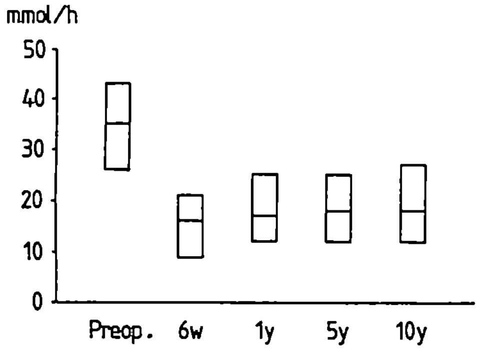

Figure 3 *Peak acid output pre- and postoperatively after stimulation with pentagastrin. Median and interquartile range shown. There is a significant decrease between the pre-operative value and the six week value* ($P<0.0001$) *and a significant increase between the 6 week and 1 year value* ($P<0.01$)

prepyloric or pyloric ulcer have had a recurrence (*Figure 1*). Nine out of the sixteen patients primarily operated upon because of duodenal ulcer had their recurrences in the duodenal cap, the remaining in the prepyloric region ($n=4$) or in the antral region ($n=3$). Both patients with primarily prepyloric ulcer disease had their recurrences in the prepyloric region. Four patients have been re-operated with vagotomy and pyloroplasty, one with a 'second PCV'[14] and one with a pyloroplasty. At the 10 year follow-up 14 patients had slight to moderate symptoms of epigastric pain without any signs of ulcer recurrence. A complaint of slight nausea without incapacitating dumping was shown in six patients and six patients had a tendency to looser bowel movements after surgery compared to the state before surgery. However, 89 per cent of all patients were satisfied with the results of the operation.

Basal acid output was reduced by 75 per cent at the 6 week follow-up. During the first year there was a significant increase ($P<0.01$) in basal acid output but it remained stable thereafter (*Figure 2*). The peak acid output after pentagastrin stimulation was reduced by 50 per cent after vagotomy it then increased during the first year and was stable thereafter (*Figure 3*). The peak acid output after insulin stimulation increased during the first 5 years but remained unchanged at the 10 year follow-up (*Figure 4*).

Vitamin B_{12} values decreased significantly ($P<0.05$) during the 10 year period but were still within the normal range. Patient weight was slightly but significantly increased (pre-operative and 10 year weight being 71 and 74 kg respectively, $P<0.05$. The serum values of haemoglobin, serum calcium and serum iron remained unchanged during the first 10 years after surgery.

Discussion

In this study, we report the outcome of 100 patients 10 years after PCV. No operative mortality was found and the frequency of postoperative complaints was negligible. Although an 18 per cent recurrence rate was found, 89 per cent of all patients were satisfied with the result of the operation. The frequency of non-symptomatic recurrences in this series is unknown. After 5 years a recurrence rate of 14 per cent (of which approximately 50 per cent were asymptomatic) has been reported[16]. No changes in gastric acid secretion occurred after 5 years and we did not find any negative changes in the metabolic parameters. How do these figures compare to other surgical procedures used for duodenal ulcer disease? In comparing recurrence rates between different surgical methods it has to be remembered that older studies were performed before the technique of double-contrast radiological examinations was introduced and also before the era of upper gastrointestinal endoscopy. Thus, the indications for surgery could not be established with the same accuracy as today. Also, a recurrence was difficult to diagnose, especially after partial gastrectomy using the old radiological technique. Despite these facts, after partial gastric resection with or without vagotomy and also after truncal vagotomy and drainage, the recurrence rates are considerably lower than the recurrence rate 10 years after PCV. In a 25-year follow-up, Fischer found a 2·4 per cent recurrence rate after Billroth II resection[1], O'Leary[17] found a 5·7 per cent recurrence rate 6 years after vagotomy and drainage and 25 years after vagotomy and antrectomy a 0·6 per cent recurrent rate has been reported[18].

In the Aarhus vagotomy trial[8] a higher number of recurrences was found among those with prepyloric/pyloric ulcer disease. We cannot explain the low recurrence rate in this study in patients operated upon because of this disease, but it could be due to the fact that this group consists of only 29 patients.

The important facts that the operative mortality and the frequency of postoperative sequelae are considerably lower after PCV than after any other surgical procedure used for duodenal ulcer disease stands in favour for PCV. Mortality during surgery for a benign condition or the creation of disabling symptoms after surgery, known to be resistant to further surgical therapy[19], is a disaster.

The gradual increase in gastric acid production, which was revealed during the first 5 years, did not continue during the latter part of the follow-up period. This indicates that, if reinnervation of the stomach is the mechanism of the increased acidity after PCV, it takes place during the first years after surgery. However, new recurrences do occur between the 5 and

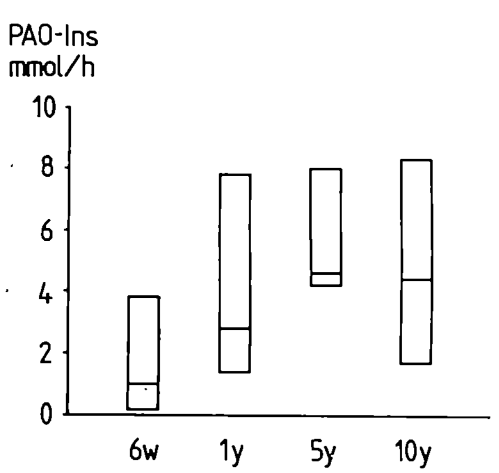

Figure 4 *Peak acid output after insulin stimulation. Median and interquartile range shown. There is a significant increase between the 6 week and 1 year value and also between the 1 year and 5 year value (both* $P<0.01$)

the 10 year follow-up, which substantiate our opinion that the gradual increase in gastric acid secretion is of minor importance in recurrent disease. Perhaps a reduction of the mucosa to resist ulceration is important. The risk of new recurrences in a perspective longer than 10 years ought to be low.

We have not been able to detect any metabolic changes among our patients which can be referred to the operative procedure and the slight decrease in vitamin B_{12} value are in accordance with a normal non-ulcer population[20]. On the contrary, after partial gastrectomy anaemia, hypocalcaemia, hypo-albuminaemia and weight loss are common phenomena occurring in 7–18 per cent of the patients[1].

To our knowledge, three randomized studies are available comparing H_2-receptor antagonists and PCV. In the study by Ström *et al.*[21] PCV was compared to a 3 year maintenance regimen of cimetidine 400 mg at bed-time. In the PCV group 7 out of 32 (22 per cent) duodenal ulcer patients experienced recurrences as compared to 15 out of 33 (46 per cent) in the cimetidine group. In a Danish study[22] maintenance therapy with 400 mg cimetidine daily for one year was compared to PCV. During a mean follow-up period of 57 months 38 per cent of the patients in the cimetidine group ($n = 45$) had recurrences as compared to 8 out of 41 (20 per cent) patients randomized to PCV. In the third study by Gear[23] indefinite maintenance therapy with 400 mg cimetidine was compared to PCV and 54 per cent in the group treated with cimetidine ($n = 24$) developed a recurrence as opposed to 10 per cent in the PCV group ($n = 20$). With these studies as background we regard the recurrence rate after PCV as acceptable and since the operative procedure has a very low rate of postoperative sequelae it seems appropriate to consider PCV as the method of choice in chronic duodenal ulcer disease.

Acknowledgements

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References

1. Fischer AB. Twenty-five years after Billroth II gastrectomy for duodenal ulcer. *World J Surg* 1984; **8**: 293–302.
2. Goligher J. Pulvertaft C, de Dombal F, *et al.* Five-to-eight-year results of Leeds/York controlled trial of elective surgery for duodenal ulcer. *Br Med J* 1968; **2**: 781–7.
3. Stabile B, Passaro E Jr. Recurrent peptic ulcer. *Gastroenterology* 1976; **70**: 124–35.
4. Johnston D, Wilkinson A. Selective vagotomy with innervated antrum without drainage procedure for duodenal ulcer. *Br J Surg* 1969; **56**: 626.
5. Amdrup E, Jensen HE. Selective vagotomy of the parietal cell mass preserving innervation of the undrained antrum. *Gastroenterology* 1970; **59**: 522–7.
6. Johnston D. Operative mortality and postoperative morbidity of highly selective vagotomy. *Br Med J* 1975; **5**: 545–7.
7. Muller C, Engelke B, Fiedler L *et al.* How do clinical results after proximal gastric vagotomy compare with the Visick grade pattern of healthy controls? *World J Surg* 1983; **7**: 610–5.
8. Andersen D, Amdrup E, Höstrup H, Hanberg Sörensen F. The Aarhus county vagotomy trial: trends in the problem of recurrent ulcer after parietal cell vagotomy and selective gastric vagotomy with drainage. *World J Surg* 1982; **6**: 86–92.
9. Nilsell K. Five to nine years results of selective proximal vagotomy with and without pyloroplasty for duodenal ulcer. *Acta Chir Scand* 1979; **145**: 251–5.
10. Jensen HE, Amdrup E. Follow-up of 100 patients five to eight years after parietal cell vagotomy. *World J Surg* 1978; **2**: 525–32.
11. Goligher J, Hill G, Kenny T, Nutter E. Proximal gastric vagotomy without drainage for duodenal ulcer: results after 5–8 years. *Br J Surg* 1978; **65**: 145–51.
12. Madsen P, Kronborg O. Recurrent ulcer $5\frac{1}{2}$–8 years after highly selective vagotomy without drainage and selective vagotomy with pyloroplasty. *Scand J Gastroenterol* 1980; **15**: 193–9.
13. Graffner H, Liedberg G, Oscarson J. Parietal cell vagotomy in the surgical treatment of chronic duodenal, pyloric and prepyloric ulcer disease. *Int Surg* 1985; **70**: 139–44.
14. Graffner H, Liedberg G, Oscarson J. Recurrence after parietal cell vagotomy for peptic ulcer disease. *Am J Surg* 1985; **150**: 336–40.
15. Graffner H, Liedberg G, Oscarson J. Acid secretory tests in peptic ulcer disease before and after parietal cell vagotomy. *Scand J Gastroenterol* 1986; **21**: 41–6.
16. Baron J, Alexander-Williams J, Allgöwer M, Muller C, Spencer J. *Vagotomy in Modern Surgical Practice.* London: Butterworths, 176–86, 1982.
17. O'Leary J, Woodward E, Hollenbeck J, Dragstedt L. Vagotomy and drainage procedure for duodenal ulcer: The result of seventeen years' experience. *Ann Surg* 1976; **183**: 613.
18. Herrington L Jr, Sawyers J, Scott W Jr. A 25-year experience with vagotomy-antrectomy. *Arch Surg* 1973; **106**: 469–74.
19. Ritchie WP Jr. Alkaline reflux gastritis: A diagnosis in search of a disease? *Can J Surg* 1982; **25**: 248–9.
20. Borgström B, Nordén Å, Åkesson B, Abdulla M, Jägerstad M. Nutrition and old age. Chemical analyses of what old people eat and their state of health during six years of follow-up. *Scand J Gastroenterol* 1979; **14**(Suppl. 52): 191–5.
21. Ström M, Lindhagen J, Bodemar G, Sjödahl R, Walan A. Cimetidine or parietal-cell vagotomy in patients with juxtapyloric ulcers. *Lancet* 1984; **20**: 894–7.
22. Harling H, Balslev I, Bentzen E. Parietal cell vagotomy or cimetidine maintenance therapy for duodenal ulcer? A prospective controlled trial. *Scand J Gastroenterol* 1985; **20**: 747–50.
23. Gear MWL. Proximal gastric vagotomy versus long-term maintenance treatment with cimetidine for chronic duodenal ulcer: a prospective randomised trial. *Br Med J* 1983; **286**: 98–9.

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Effect of cimetidine on prognosis after simple closure of perforated duodenal ulcer

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A prospective controlled study in 60 patients undergoing simple closure of perforated duodenal ulcer demonstrated a significant ($P<0.05$) *benefit following postoperative cimetidine treatment, in terms of avoiding subsequent dyspeptic symptoms and complications of peptic ulcer disease. Thus cimetidine is recommended in the follow-up management of perforated duodenal ulcers.*

Keywords: Duodenal ulcer, perforation, postoperative cimetidine treatment

The introduction of effective medical treatment for duodenal ulcer with cimetidine has significantly reduced the rate of elective ulcer surgery[1,2]. The management of a perforated duodenal ulcer remains a surgical problem but the availability of cimetidine offers the opportunity to re-appraise the role of simple closure in the treatment of perforated duodenal ulcer. The efficacy of cimetidine following simple closure has been assessed in a prospective controlled clinical study.

Patients

A series of 60 consecutive patients with perforated duodenal ulcer were treated by simple closure, with an omental patch, during the period 1 January 1982 to 31 December 1983. The patients were randomized, by drawing a card in theatre, to receive cimetidine postoperatively or to a control group. Cimetidine was administered in a daily dose of 1·6 g intravenously for 48 h, then 1 g daily orally for 8 weeks, followed by 400 mg at night to 26 weeks after the operation. The control group did not receive any specific anti-ulcer therapy. Patients were reviewed as out-patients at 1, 2, 6 and 12 months and endoscopy was performed when symptoms occurred.

Thirty patients were randomized to each group without significant differences between the groups in terms of age, sex ratio, dyspeptic history, previous cimetidine therapy, cigarette smoking or time interval from perforation to operation (*Table 1*). Patients with a dyspeptic history >3 months were considered to have chronic duodenal ulceration. Eight of twenty-eight with 'acute' ulcers admitted to the ingestion of non-steroidal anti-inflammatory drugs in the 2 weeks before surgery. Statistical analysis of the results was performed using the χ^2 test with Yates' correction. Patients were informed of the nature of the study and the design of the trial was accepted by the hospital ethical committee.

Results

Mortality

Eight patients died within one month of surgery, only one being less than 64 years old (*Table 2*). Cimetidine therapy did not influence mortality. The time interval from perforation to surgery did not appear to influence mortality but it must be emphasized that the number of patients with a significant delay before operation (>12 h) was very small.

Recurrent symptoms

Cimetidine treatment did confer significant benefit in apparently completely preventing ulcer symptoms in the year following perforation. Three patients, in the control group, none of whom had been taking cimetidine before perforation, required further definitive surgery, one for a second perforation and two for bleeding duodenal ulceration. A further eight patients, two defined as having acute ulcers at the time of surgery, developed clinical and endoscopic evidence of active ulcer disease within 7 months of perforation. There was no change in cigarette consumption in either group at follow-up despite advice being given to discontinue smoking.

Discussion

The incidence of perforated peptic ulcer in the West of Scotland has declined since the 1950s[3], but this decline does not appear to have been accelerated by the introduction of cimetidine[4]. Perforation does remain a potentially fatal complication of duodenal ulcer, especially in the elderly, and the mortality in the present study is similar to earlier reports from this region[5].

Table 1 *Clinical data*

	Cimetidine	Control
Age (in years) mean ± s.d.	52 ± 3·7	58 ± 3·3
Time interval until surgery		
<4 h	4	4
4–12 h	24	22
>12 h	2	4
Cigarette smoking		
None	8	13
<20 per day	9	5
>20 per day	13	12
Dyspeptic history		
None	5	6
<3 months	8	9
>3 months	17	15
Cimetidine therapy	6	6

Table 2 *Operative mortality*

Cimetidine group
- 3 deaths (10 per cent)
- Postoperative days (2–14)
  - Myocardial infarction (age 64)
  - Multiple organ failure (age 75)
  - Acute renal failure (age 71)

Control group
- 5 deaths (16·6 per cent)
- Postoperative days 2–19
  - Myocardial infarction (age 81)
  - Bronchopneumonia (age 82)
  - Multiple organ failure (age 51)
  - Cerebrovascular accident (age 64)
  - Acute renal failure (age 70)

Mortality
- ⩾65 years 5/18 (27%)
- <65 years 3/42 (7%)

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Surgical opinion, however, has remained divided as to the optimum management of perforated duodenal ulcers, between simple closure alone and concomitant definitive ulcer surgery[6]. The lower mortality anticipated following the lesser procedure has not always been confirmed in clinical studies[7].

Both truncal vagotomy with drainage and proximal gastric vagotomy proved safe in a prospective study of perforated chronic duodenal ulcers from which patients who were elderly or had significant medical illness were excluded[8]. The third group in this last study, who had simple closure alone, had a 63 per cent incidence of recurrent ulceration at subsequent endoscopy. The incidence of recurrent dyspeptic symptoms following simple closure has varied from 24 to 69 per cent[7,9,10], and the inadequacy of simple closure has again been demonstrated in this study.

A selective policy of surgical management, offering definitive surgery for patients with chronic ulceration, in the absence of severe cardiorespiratory disability, leaving simple closure for the high risk patient and patients with perforated acute ulcers, appears attractive. Definition of chronicity of an ulcer, however, is imprecise and differentiating between acute and chronic ulceration may be difficult. Subsequent review of pre-operative data used to categorize perforated ulcers identified significant errors in almost 50 per cent of 112 patients, which could have led to inappropriate surgery[11]. Similarly, separating the acute from chronic ulcer at operation is not always clear-cut, especially as most perforations in the UK are managed by surgeons in training. Definitive surgery has been shown to be both safe and effective in selected patients but it will be unnecessary in an unpredictable but significant proportion of patients.

Cimetidine has proved very effective in preventing symptomatic recurrence and ulcer complaints in the present study. The early results suggest a need to re-assess the role of definitive surgery for perforation. Although recurrent dyspepsia following simple suture commonly occurs within 12 months[11] and indeed occurred within 7 months in this study, longer follow-up will help to assess the relative merits of cimetidine treatment and the data on definitive surgery. The early results are encouraging and although successful ulcer healing cannot be claimed in the absence of endoscopy, there is no doubting the excellent symptomatic benefit. The number of patients with acute ulcers is too small to identify the role of cimetidine therapy in this group. The incidence of dyspeptic symptoms and ulcer complications following simple closure of a perforated ulcer is too great to endorse such a policy alone.

Cimetidine therapy following simple closure avoids any difficulty in selecting patients for definitive surgery at the time of perforation, in terms of ulcer chronicity and assessment of cardiorespiratory disability, and can be recommended in the follow-up management of perforated duodenal ulcer.

References

1. Fineberg HV, Pearlman LA. Surgical treatment of peptic ulcer in United States. *Lancet* 1981; **i**: 1305–7.
2. Wylie JH, Clark CG, Alexander-Williams J, Bell PRF, Kennedy TL, Kirk RM, MacKay C. Effect of cimetidine on surgery for duodenal ulcer. *Lancet* 1981; **i**: 1307–8.
3. MacKay C. Peforated peptic ulcer in the West of Scotland: a survey of 5343 cases during 1954–1963. *Br Med J* 1966; **1**: 701–2.
4. MacKay AJ, McArdle CS. Cimetidine and perforated peptic ulcers. *Gut* 1981; **22**: A880.
5. MacKay C, MacKay HP. Perforated peptic ulcer in the West of Scotland 1964–1967. *Br J Surg* 1976; **63**: 157.
6. Drury JK, MacKay AJ, Hutchison JSF, Joffe SN. Natural history of perforated duodenal ulcers treated by suture closure. *Lancet* 1978; **ii**: 749–50.
7. Sawyers JL, Herrington JL Jr, Mulherin JL, Whitehead WA, Mody B. Acute perforated duodenal ulcer. *Arch Surg* 1975; **110**: 527–30.
8. Boey J, Lee NW, Koo J, Lam PHM, Wong J, Ong GB. Immediate definitive surgery for perforated duodenal ulcers. *Ann Surg* 1982; **196**: 338–44.
9. Wangensteen SL, Wray RC, Golden GT. Perforated duodenal ulcer. *Am J Surg* 1972; **123**: 538–42.
10. Hennessy EJ, Chapman BL, Duggan JM. Peforated peptic ulcer long term follow up. *Med J Aust* 1976; **1**: 50–3.
11. Baekgaard N, Lawaetz O, Ejby Poulsen P. Simple closure or definitive surgery for perforated duodenal ulcer. *Scand J Gastroent* 1979; **14**: 17–20.

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Maximal gastric secretion and duodenogastric reflux in patients with gastric or duodenal ulcer and in control subjects

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Maximal gastric secretion was studied in 41 unoperated patients with gastric ulcer, 201 patients with duodenal ulcer, and 122 control subjects. The patients with a gastric ulcer were divided into high, body and prepyloric, according to the site of the ulcer. Both high and body gastric ulcers secreted significantly less than the controls, and the duodenal ulcer patients secreted significantly more. However, the patients with gastric ulcer were older and lighter than the controls and, since these factors are known to influence maximal gastric secretion, the controls and patients with duodenal ulcer were standardized to the mean weight (and age, for the controls) of the gastric ulcer group. After this standardization, there was no significant difference in secretion between the patients with body ulcers and normal controls. Pyloric loss was a similar percentage of maximal gastric secretion in all groups, but duodenogastric reflux was higher in the gastric ulcer group compared to the controls. The mean volume of duodenogastric reflux was greatest in the patients with a prepyloric gastric ulcer. It is commonly accepted that hyposecretion in patients with a gastric ulcer is due to gastritis consequent upon increased duodenogastric reflux. However, in this study, no gastric hyposecretion was evident in the body and prepyloric gastric ulcer groups, both of whom had greater than normal levels of duodenogastric reflux.

Keywords: Gastric ulcer, duodenal ulcer, gastric secretion, duodenogastric reflux

It is generally accepted that gastric ulcers (GU) are associated with abnormal secretory patterns. The results of earlier studies[1,2] showed that the higher the ulcer in the stomach, the lower the gastric secretion. This hyposecretion was assumed to be due to a reduced parietal cell mass, itself due to atrophic gastritis caused by increased bile reflux[3,4]. It has also been suggested that reflux itself is an aetiological factor for gastric ulcer[5], although there is controversy about the magnitude and occurrence of duodenogastric reflux in patients with gastric ulcer and the normal population[6–8]. In the present study we examined the maximal gastric secretion, reflux and pyloric loss in patients with gastric ulcer, duodenal ulcer (DU), and control subjects.

Patients and methods

Gastric secretion studies were performed in 41 unoperated patients with gastric ulcer (GU) (18 men and 23 women), 122 control subjects (79 men and 43 women), and 201 patients with unoperated duodenal ulcer (DU) (146 men and 55 women). The diagnosis of GU or DU had been confirmed by endoscopy, or at operation. Gastric ulcers were categorized as prepyloric, body (at or just above the incisura), or high (at or near the gastro-oesophageal junction). All of the duodenal ulcers were in the first part of the duodenum. The controls were healthy staff or in-patients without or with gastrointestinal complaints, the latter without peptic ulcer as proved by appropriate investigation.

Each subject fasted from midnight and abstained from any medication. The following morning the subject was placed on a couch in a semi-recumbent position, and a special two-lumen nasogastric tube was passed into the stomach, with the position of the tube verified by the water recovery test[9]. In all subjects phenol red (6 g l^{-1}) was instilled into the stomach through the smaller lumen tube at a rate of 10·6 ml h^{-1} in order to assess pyloric loss of gastric juice. After a collection of basal secretion for at least half an hour, histamine acid phosphate was given by continuous intravenous infusion, at a rate of 130 nmol kg^{-1} h^{-1} in order to stimulate maximal gastric secretion. The observed volume of gastric secretion (V_{obs}) was corrected for pyloric losses, to give V_{cor}, and further corrected for duodenogastric reflux to give V_g (ml h^{-1}). The plateau of maximal gastric secretion was selected using an objective method, and maximal gastric secretion was expressed as acid output (*AO*, mmol h^{-1}) and V_g (ml h^{-1}). The volume of pyloric loss was calculated by using phenol red as a dilution indicator, and the volume of reflux was calculated using a formula based on the output of sodium ions. Full details of the test technique and calculations have been published[10].

Regression analysis was by the method of least squares, with the significance of the coefficients judged by the *t* test. The statistical significance of differences between groups was tested by Student's *t* test for unpaired data, using the form for unequal variances. Medians are also given.

Results

Maximal gastric secretion

Eight patients (3 men and 5 women) had a prepyloric ulcer. Three patients (2 men and 1 woman) had a high GU on or near the gastro-oesophageal junction, and in 30 patients (13 men and 17 women), the ulcer was located at or above the incisura angularis, in the body of the stomach. The means and standard deviations of the maximal gastric secretion of these three groups are given in *Table 1*, with the values of the control and DU patients for comparison. The high group consisted of the three lowest secretors, and their mean secretion was significantly less ($P < 0·001$) than that of the patients with body ulcers, who in turn secreted significantly less ($P < 0·001$) than the control group. The prepyloric group included the two highest secretors of the GU group, but the group as a whole did not secrete significantly more than the control group. The DU patients secreted significantly more than the controls.

Differences in age, height, and weight between GU patients, DU patients, and controls (Table 2)

The mean age of the patients with gastric ulcer was significantly greater ($P < 0·001$) than that of controls, whereas the mean

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Table 1 *Comparison of maximal gastric secretion*

		High (n=3)	Body (n=30)	Controls (n=122)	Prepyloric (n=8)	Duodenal ulcer (n=201)
AO (mmol h^{-1})	mean	4·0	17·5	25·8	25·3	35·9
	s.d.	2·3	7·7	12·9	13·7	14·9
	median	4·9	16·2	23·5	25·9	35·5
V_g (ml h^{-1})	mean	62·6	191·2	253·1	274·9	357·9
	s.d.	30·3	66·1	115·1	119·2	136·9
	median	69·6	173·4	237·6	242·4	332·4

Table 2 *Comparison of mean age, height and weight in controls, gastric ulcer patients and duodenal ulcer patients*

	Gastric ulcers	Control	Duodenal ulcers
Mean age (years)	53·6	42·9	45·3
s.d.	12·5	15·4	13·9
Mean weight (kg)	56·9	65·0	65·8
s.d.	11·8	10·8	13·1
Mean height (cm)	164·9	170·1	169·4
s.d.	8·4	10·7	8·9

Table 3 *Single and multiple regressions of gastric secretion results*

Acid output (mmol h^{-1})		
Controls	: 0·328 * weight − 0·26 * age + 15·30	r=0·47
GU	: 0·297 * weight + 0·93	r=0·32
DU	: 0·330 * weight + 14·26	r=0·27
Aspirated volume (V_{obs}) (ml h^{-1})		
Controls	: 2·18 * weight − 1·76 * age + 155·2	r=0·48
GU	: 2·79 * weight + 27·5	r=0·37
DU	: 2·44 * weight + 137·1	r=0·30
V_g (ml h^{-1})		
Controls	: 2·79 * weight − 1·98 * age + 153·0	r=0·44
GU	: 2·54 * weight + 50·4	r=0·27
DU	: 3·73 * weight + 111·2	r=0·32

GU, gastric ulcer patients; DU, duodenal ulcer patients

height and weight were significantly less (P<0·005). The DU group did not differ from the controls in these respects. It was therefore necessary, if possible, to correct for the differences between the controls and DU group on the one hand, and the GU group.

Relationship of secretion with height, weight and age (Table 3)

Gastric ulcer. V_g and AO were analysed for possible correlation with height, weight, and age in the GU group. Both indices of maximal gastric secretion were found to have statistically significant positive correlations with weight. There was no significant correlation between maximal secretion and age or height.

Control group. V_g and AO were found to have statistically significant correlations with height, weight, and age, and there were significant multiple regressions with height and age, and weight and age for AO and V_g.

Duodenal ulcer. V_g and AO were found to have statistically significant correlations with height or weight.

The V_g and AO of the controls were standardized to the mean weight and age of the GU group, and the DU and GU groups were standardized to the mean weight of the GU group by their respective equations.

Differences in secretion after weight- and age-standardization (Table 4 *and* Figure 1)

The patients with high gastric ulcers still secreted significantly less (P<0·001) than the patients with body ulcers. However, this latter group did not now differ significantly from the control group. The prepyloric group occupied an intermediate position, in terms of gastric secretion, between the control group and the DU group, but did not differ significantly from either group.

Differences in pyloric loss and duodenogastric reflux (Table 4)

Pyloric losses increased as maximal secretion increased, and was an approximately constant percentage (14–24 per cent) of V_g.

Duodenogastric reflux was very much the same in the patients with high and body ulcers (19 ml h^{-1}), less in the controls and DU patients (6–12 ml h^{-1}), but highest in the patients with prepyloric ulcers (37 ml h^{-1}). As a group, the patients with high and body ulcers had significantly greater reflux than the controls (t=2·9, P<0·01). The patients with prepyloric ulcers also had significantly greater reflux than the controls (t=4·2, P<0·01), the DU patients (t=3·6, P<0·01), and the other GU patients (t=2·5, P<0·05). The duodenal ulcer patients did not have significantly greater levels of reflux than the controls (t=1·3, P=0·20) (*Figure 2*).

Discussion

The initial results of this study appeared to show that the maximal gastric secretion of patients with high or body gastric ulcers was

Table 4 *Weight- and age-standardized maximal gastric secretion*

		High	Body	Control	Prepyloric	Duodenal ulcers
	n	3	30	122	8	201
Weight-standardized AO (mmol h^{-1}) (and age for controls)	mean	0·80	18·60	20·09	23·10	32·05
	s.d.	2·13	7·17	11·27	11·65	14·19
	median	0·40	17·3	19·33	25·10	31·1
Weight-standardized V_g (ml h^{-1}) (and age for controls)	mean	35·5	198·7	206·1	262·2	318·6
	s.d.	18·75	66·2	90·0	97·1	128·7
	median	43·1	189·7	202·8	248·9	303·6
Pyloric loss (ml h^{-1})	mean	7·2	28·4	35·3	58·9	75·5
	s.d.	15·7	48·7	49·1	69·2	82·0
	median	15·6	24·1	27·3	55·5	52·2
Percentage of V_g		20·3	14·3	17·1	22·5	23·7
Duodenogastric reflux (ml h^{-1})	mean	19·4	19·0	6·3	36·6	11·8
	s.d.	16·6	16·5	36·5	18·0	36·6
	median	15·0	17·7	−1·2	39·3	1·8
Percentage of V_g		54·6	9·8	−0·6	14·0	3·7

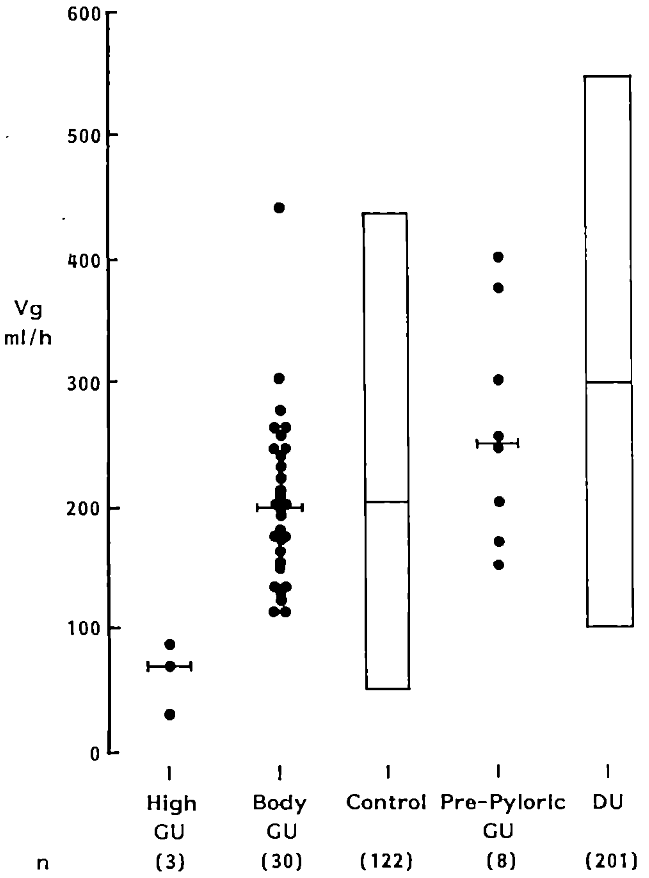

Figure 1 *Weight-standardized maximal gastric secretion (V_g, ml h^{-1}). Bars are medians or 95 per cent range*

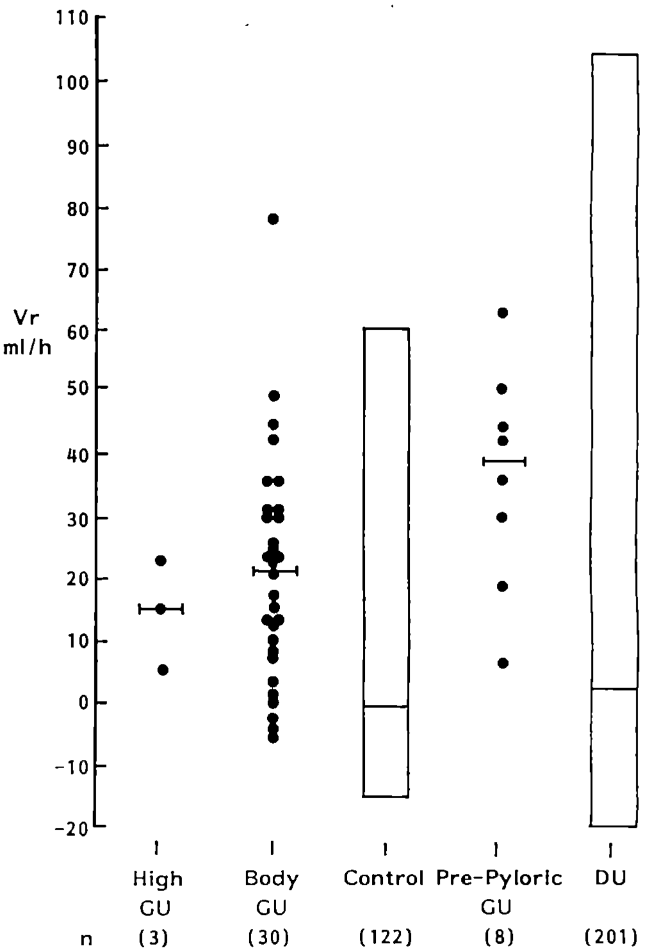

Figure 2 *Duodenogastric reflux (V_r) during maximal gastric secretion. Bars are medians or 95 per cent range*

less than in controls. However, the patients with gastric ulcer were, as a group, significantly older, shorter and lighter than the controls and, since it is known that age, height and weight influence maximal gastric secretion in controls[11], the gastric secretion of the control group was standardized to the mean age and weight of the GU group. After this standardization, no significant difference was found between patients with a body ulcer and the control sample. We did not find, as others have done, that the patients with a prepyloric ulcer had a significantly raised maximal gastric secretion, although they did occupy an intermediate position between the controls and DU patients. We did find, though, that the patients with high gastric ulcer had a significantly lower gastric secretion than that of those with a body ulcer or of the controls. The maximal secretion rate of the high ulcer group was very low, indeed at basal levels, a fact that is suggestive of a very small parietal cell mass.

Pyloric losses broadly reflected the rate of gastric secretion of each group, with perhaps a hint of a lower rate of loss in those patients with a body ulcer.

The finding of no significant difference in maximal gastric secretion between controls and patients with a body ulcer seems to be in contrast with the conclusions of previous studies but there are a number of reasons why the latter are suspect. For example, Aubrey and Forrest[12] reported that the output of acid in GU patients after histamine stimulation was lower than in normal controls, but no correction had been made for errors due to pyloric losses and duodenogastric reflux[13]; and no allowances made for stature and age[11]. Moreover, without corrections for pyloric losses and duodenogastric relfux, the titratable acidity (which is strongly affected by the alkaline duodenogastric reflux) is not a good index of gastric secretion[14]. The method used in the present study takes into account all the factors, except swallowed saliva, that are known to influence the measurement of gastric secretion. Volume was corrected for pyloric loss and duodenogastric reflux and standardized for age and stature[15].

Increased bile reflux has been suggested as a cause of gastric ulcer[5]. Later studies[3,4] claimed that increased bile reflux is a characteristic of GU. However, it must be noted that the difference found was of borderline significance, $P = 0{\cdot}05$[3] and that increased bile reflux was not found in all GU patients[4]. In that same study[4], there was an overlap of values among normal, patients with duodenal ulcer, and patients with gastric ulcer. The results of other studies[6–8] did not confirm these early findings. Recent work[16] comparing endoscopic findings of reflux with the results of scintigraphic assessment of reflux showed that the reflux was 0–5 per cent in normal controls without endoscopic evidence of reflux and 0–16 per cent in patients with endoscopic findings of reflux, but only two out of ten subjects studied had values outside the normal range. Thus, the evidence for increased reflux in patients with GU is not very strong.

In this study, duodenogastric reflux has been measured by using the sodium concentration of the aspirated gastric juice as a marker of reflux contamination of the gastric juice. High levels of sodium, over and above that expected for controls, signifies extra reflux. The measure of reflux in this study is therefore not absolute, but represents the quantity above the norm. The method is independent of bile concentration and changes in gastric secretion. It also avoids transpyloric intubation which may by itself induce reflux, and the technique has an excellent correlation with the method which uses an inert marker in the duodenum[17]. The results show that the extra volume of duodenogastric reflux in the patients with gastric ulcer was significantly higher than in the controls, especially in the prepyloric group. Bile acid concentrations have also been reported to be higher in patients with prepyloric gastric ulcer than in controls[18]. Duodenogastric reflux was not greater than the controls in the duodenal ulcer group.

Our results support the hypothesis of an association between gastric ulcer and duodenogastric reflux. They do not support any association between duodenogastric reflux and hyposecretion. Although the group with the greatest degree of hyposecretion, the patients with high gastric ulcers, did have high levels of reflux, patients with gastric ulcers elsewhere in the stomach had similar or higher levels of reflux, but demonstrated no hyposecretion. This leaves unclear the aetiology of the marked hyposecretion (down to basal levels) of the patients with high gastric ulcers.

References

1. Grossman MI, Kirsner JB, Gillespie I. Basal and Histalog-stimulated gastric secretion in control subjects and in patients with peptic ulcer or gastric cancer. *Gastroenterology* 1963; **45**: 14–26.
2. Baron JH. *Clinical Tests of Gastric Secretion.* London: Macmillans, 1978, 86–91.
3. Rhodes J, Barnardo DE, Phillips SF, Rovelstad RA, Hofmann AF. Increased reflux of bile into the stomach in patients with gastric ulcer. *Gastroenterology* 1969; **57**: 241–52.
4. Wormsley KG. Aspects of duodenogastric reflux in man. *Gut* 1972; **13**: 243–50.
5. Du Plessis DJ. Pathogenesis of gastric ulceration. *Lancet* 1965; **i**: 975–8.
6. Dupas JL, Papazian A, Capron JP, Gineston JL, Lorriaux A. Pyloric bilirubin outputs: a new method for evaluation of duodenogastric reflux. *Scand J Gastroent* 1981; **16**(Suppl 67): 47–50.
7. Hollinger A, Ammann R, Sioller G, Pellika R. Quantitative assessment of duodenogastric reflux after vagotomy with or without pyloroplasty. A clinical investigation. *Scand J Gastroent* 1981; **16**(Suppl 67): 55–7.
8. Muller-Lisner A, Sonnenberg A, Muller-Duysing W, Blum AL. Quantitative measurement of duodenogastric reflux in man. *Scand J Gastroent* 1981; **16**(Suppl 67): 179.
9. Hassan MA, Hobsley M. Positioning of subject and of nasogastric tube during a gastric secretion study. *Br Med J* 1970; **i**: 458–60.
10. Whitfield PF, Hobsley M. A standardised technique for the performance of accurate gastric secretion studies. *Agents and Actions* 1978; **9**: 327–32.
11. Hassan MA, Hobsley M. The accurate assessment of maximal gastric secretion in control subjects and patients with duodenal ulcer. *Br J Surg* 1971; **58**: 171–9.
12. Aubrey DA, Forrest APM. Effects of histamine acid phosphate and pentagastrin on gastric secretion in normal human subjects and in patients with various gastroduodenal diseases. *Ann Surg* 1971; **174**: 866–79.
13. Faber RG, Hobsley M. Basal gastric secretion: reproducibility and relationship with duodenal ulceration. *Gut* 1977; **18**: 57–63.
14. Faber RG, Russell RCG, Parkin JV, Whitfield P, Hobsley M. The predictive accuracy of the postvagotomy insulin test: a new interpretation. *Gut* 1975; **16**: 337–42.
15. Maybury NK, Faber RG, Hobsley M. Postvagotomy insulin test: improved predictability of ulcer recurrence after corrections for height and collection errors. *Gut* 1977; **88**: 449–56.
16. Eyre-Brook IA, Holroyd AM, Johnson AG. Is bile reflux at endoscopy a significant finding? *Scand J Gastroent* 1984; **19**(Suppl 92): 203–5.
17. Fiddian-Green RG, Russell RCG, Hobsley M. Secretin-induced pyloric reflux: verification of the mathematical formula for eliminating reflux in gastric aspirate. *Br J Surg* 1972; **59**: 903.
18. Gotthard R, Bodemar G, Tjadermo M, Tobiasson P, Walan A. High gastric bile acid concentration in prepyloric ulcer patients. *Scand J Gastroent* 1985; **20**: 439–46.

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Announcement

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Perisplenitis and perinephritis in the Curtis–Fitz-Hugh syndrome

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Four cases of the Curtis–Fitz-Hugh syndrome diagnosed laparoscopically and with microbiological or serological evidence of chlamydial pelvic infection are reviewed. The case histories emphasize the part played by renal angle and left upper quadrant symptoms. In one patient the surface of the spleen was affected by the same classical imflammation normally seen on the surface of the liver. In 3 patients bilateral or left-sided renal angle pain and tenderness constituted the presenting features, or a major manifestation, and in all patients renal tract investigations were entirely normal. The patient with laparoscopic perisplenitis also had perihepatitis and pelvic inflammation, the latter being florid in all cases. Perisplenitis and perinephritis are proposed as possible additional manifestations of this syndrome.

Keywords: Curtis–Fitz-Hugh syndrome, perihepatitis, perisplenitis, perinephritis

The Curtis–Fitz-Hugh syndrome of pelvic infection in association with perihepatitis has been recognized since 1919 when these characteristics were first presented to the Society of Obstetricians and Gynaecologists of Montevideo in Uraguay by Carlos Stajano[1]. Curtis[2] and Fitz-Hugh[3] in the early 1930s described in greater detail the laparotomy findings but it was not until the advent of the widespread use of laparoscopes that the relative frequency of the upper abdominal manifestations of pelvic inflammatory disease started to be effectively recognized. *Neisseriae gonorrhoeae* was considered responsible for most of the early cases, but since 1978 *Chlamydia trachomitis* has been found to be causative in an increasing number of cases[4]. Serotypes D-K which give rise to pelvic inflammatory disease are also considered responsible for perihepatic inflammation. The perihepatitis characteristic of this syndrome is usually responsible for severe right upper quadrant pain, fever and leucocytosis, closely mimicking acute cholecystitis. Furthermore the presence of parietal peritoneal inflammation affecting the underside of the diaphragm is responsible for pain referred to the right shoulder and pleuritic type right-sided chest pain mimicking pleurisy, pneumonia and pulmonary embolism[5]. Despite this, awareness of the condition remains low and many patients find themselves undergoing repeated biliary and urological investigations and, not infrequently, appendicectomy or cholecystectomy are performed in an attempt to relieve the persistent symptoms.

Case 1

A 20-year-old woman was admitted with a 3-day history of severe left loin pain and vomiting (*Table 1*). This was not associated with urinary symptomatology but had been preceded by 2 months of increasing dyspareunia and vaginal discharge. Two years previously a termination of pregnancy was complicated by the development of a serious pelvic infection which required prolonged administration of antibiotics. On examination she was pyrexial with tenderness and rigidity in the left renal angle and minimal tenderness in the suprapubic region and right upper quadrant. She had no hyperamylasaemia or leucocytosis and a presumptive diagnosis of an infected obstructed kidney was made. Emergency intravenous urography, urine microscopy and subsequent culture were entirely normal. Gradually the pain in the right upper quadrant and epigastrium became more pronounced, yet constantly overshadowed by the left loin symptoms. Upper abdominal ultrasonography, infusion cholecystography and upper gastrointestinal endoscopy were normal. At laparoscopy florid pelvic inflammatory disease was immediately evident with extensive exudates in the pouch of Douglas. The surface of the liver was streaked with inflammatory plaques and the adjacent parietal peritoneum was heavily injected. *Chlamydia trachomitis* was cultured from fluid aspirated from the pouch of Douglas and the serum antichlamydial antibody titre was elevated (*Table 2*). All her symptoms responded to a 4 week course of tetracycline.

Case 2

A 31-year-old woman presented with a 2-week history of bilateral loin pain. She had been anorexic and had vomited repeatedly. Systemic enquiry elicited a history of longstanding green vaginal discharge which had failed to respond to several courses of metronidazole and ampicillin. On examination she was pyrexial with tenderness and rigidity in both renal angles. Vaginally there was evidence of significant pelvic inflammatory disease. No leucocytosis or hyperamylasaemia were present. Urine microscopy, subsequent culture and intravenous urography were normal. Over the next 72 h her pain shifted to the right upper quadrant and she developed a positive Murphy's sign. Ultrasonography and infusion cholecystography failed to reveal

Table 1 *Clinical features of patients with Curtis–Fitz-Hugh syndrome*

		PID			Symptoms and signs		Investigations		Laparoscopic findings		
Patient no.	Age	Past	Active	TOP	RUQ	Other	Renal	Biliary	Adhesions	Perihepatitis without adhesions	PID
1	20	—	+ +	Yes	+	Left renal angle	Normal	Normal	Absent	Present	+
2	31	+ + +	+ + +	No	+ + +	Bilateral renal angle	Normal	Normal	Absent	Present	+ +
3	43	+ + +	+ + +	Yes	+ + +	Pleuritic chest pain and bilateral renal angle	Normal	Normal	Present	NA	+ + +
4	18	+ + +	+ + +	Yes	+	Left renal angle Left upper quadrant	Normal	ND	Absent	Present Perisplenitis	+ + +

+ + +, severe; + +, moderate; +, mild; –, absent

PID, pelvic inflammatory disease; TOP, termination of pregnancy; RUQ, right upper quadrant; NA, not applicable; ND, not done

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Table 2 *Results of laboratory investigations*

Patient no.	Pouch of Douglas fluid		Chylamydial antibody titres				Gonococcal complement fixation test
			Serotypes A-C		Serotypes D-K		
	Chlamydial culture	Cervical fluid culture	IgM	IgG	IgM	IgG	
1	Positive	Negative	0	0	1/64	1/512	Negative
2	Negative	Negative	0	> 1/128	0	1/128	Negative
3	Negative	Negative	0	0	1/64	1/512	Negative
4	Negative	Negative	0	0	1/64	1/512	Negative

evidence of biliary disease. Laparoscopy confirmed severe pelvic inflammatory disease and allowed visualization of numerous inflammatory white plaques on the surface of the liver and of marked injection of the pre-hepatic parietal peritoneum. Although pus cells were present in fluid aspirated from the pouch of Douglas no organisms were isolated. Serum chlamydial antibody titres were elevated to > 1/128. Her symptoms responded to tetracycline and the vaginal discharge resolved over a period of 3 months.

Case 3

A 43-year-old woman presented with a 2-day history of right sided pleuritic chest pain with referred pain to the right shoulder. She complained in addition of right-sided abdominal pain and was unwilling to breathe deeply. At the initial assessment, chest examination, radiography and electrocardiography were normal. Over the next 48 h her pain shifted to the right upper quadrant and she developed a positive Murphy's sign. Ultrasound of the liver, biliary tree and pancreas, and infusion cholecystography were normal. Repeated chest examinations and radiography were also normal. Following an apparent recovery she complained of increasing bilateral renal angle pain with vomiting. The patient remarked that these symptoms were as severe as the previous right upper quadrant symptoms. Intravenous urography, urine culture and gastroduodenoscopy were unhelpful. In view of the complicated clinical picture a laparoscopy was performed. The pelvic organs were severely inflamed with fibrin and seropurulent exudates in the pouch of Douglas. Several layers of filmy adhesions were present in the space between the liver and the anterior abdominal wall. The gallbladder and the rest of the abdominal viscera were within normal limits. No other adhesions were present. The base of the adhesions on the surface of the liver was sampled and with the same biopsy forceps the adhesions were divided to relieve the right upper quadrant symptoms. Both IgG and IgM antichlamydial titres were elevated but the organism was not isolated from the pelvic fluid (*Table 2*). Twenty-four hours after the laparoscopy the right upper quadrant pain settled and in view of the diagnosis of Curtis–Fitz-Hugh syndrome she was given a course of 4 weeks of tetracycline. She was completely asymptomatic at the last review 6 months after the laparoscopy.

Case 4

An 18-year-old woman presented with a 3-week history of increasing left upper quadrant and left loin pain. She had vomited a few times but had no urinary symptoms. Two years previously she had had a difficult termination of pregnancy, complicated by the need for evacuation of retained products of conception. This was followed by the development of a persistent vaginal discharge which failed to respond to repeated courses of antibiotics. Episodes of left renal angle and left upper quadrant pain had troubled her ever since but were never as severe as at the time of this admission. On the second day she complained of severe right upper quadrant pain and clinically she had developed a positive Murphy's sign. She had a leucocytosis of 12×10^9/l but intravenous urography, urine microscopy, urine culture and cholecystography were normal. At laparoscopy she was found to have a severely inflamed left Fallopian tube, a small left-sided ovarian cyst and extensive seropurulent exudates in the pelvis. There was obvious perihepatitis with multiple inflammatory plaques on the surface of the liver and injection of the anterior abdominal wall. The surface of the spleen was affected by an identical inflammatory process and the presplenic peritoneum was injected. The rest of the peritoneal cavity was otherwise unremarkable. She responded to 6 weeks of tetracycline and was asymptomatic 8 months after the laparoscopic examination.

Discussion

A realistic estimate of the incidence of the Curtis–Fitz-Hugh syndrome in the general population is impossible in view of its poor recognition. Furthermore, as the right upper quadrant symptoms generally dominate the picture, very little is known about other modes of presentation. Early perihepatitis involves a dry peritonitis on the surface of the liver with an appearance 'as if salt had been sprinkled on a moist surface'[3]. In more advanced cases 'violin string filmy adhesions' develop between the capsule of the liver and the anterior abdominal wall[2]. Both Curtis and Fitz-Hugh identified the association of these perihepatic changes with simultaneous active gonococcal salpingitis. In recent years, *Chlamydia trachomitis* has been found to be causative in the majority of cases[4–7]. Although most cases are indeed secondary to gonococcal and chlamydial infections, it is probable that other organisms causing pelvic infection may give rise to perihepatitis. We have recently encountered a patient with typical clinical and laparoscopic features, in whom anaerobic streptococci appeared to be responsible.

Until 1970 spread from the pelvis to the liver was assumed to be transcoelomic, particularly as diplococci had been identified in the subhepatic pouch of Fitz-Hugh's original case. However the discovery of the syndrome in a man with gonococcal septicaemia[8], in whom contiguous spread is impossible, greatly favours blood-borne infection. Evidence of past or active pelvic infection is often overshadowed by the right upper quadrant signs and symptoms and the diagnosis is only suspected when direct enquiry elicits such a history in the presence of negative biliary investigations. The length of the history is variable, but chronicity is probably the rule until the condition is recognized or the patient treated inadvertently.

The dramatic degree of left loin pain in case 1 which was confidently diagnosed as renal colic, the bilateral loin tenderness and rigidity in case 2, the acute loin pain with vomiting in case 3 and the left upper quadrant symptoms in case 4 are certainly previously unrecognized manifestations of this syndrome (*Table 1*). In all cases renal disease was reliably excluded and the symptoms responded to tetracycline therapy. The perisplenitis identified in case 4 has not been described previously, possibly because the spleen is not readily accessible for laparoscopic assessment. In all cases the renal angle or left upper quadrant symptoms and signs occurred at the same time as the perihepatitis became clinically apparent and in cases 1 and 4 represented the dominant feature. The bilateral loin pain and tenderness encountered in cases 2 and 3 suggest that the renal capsule may also be involved by the same inflammatory process. As the spread of infection is now considered to be haematogenous, the retroperitoneal position of the kidneys does not exclude such a possibility.

Confirmation of a 'perinephritis' is difficult as direct access to the kidneys for evaluation would be unjustifiably invasive. However we do feel that sexually active females with renal angle pain and tenderness and negative urological and biliary investigations warrant further assessment for evidence of chlamydial pelvic infection and laparoscopy for perihepatitis and perisplenitis. Diagnosis is particularly rewarding as many of these patients become chronic sufferers. Treatment consists of a 4 week course of tetracycline. Finally, division of the prehepatic adhesions at laparoscopy results in rapid relief of the right upper quadrant symptoms[9].

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References

1. Stajano C. La reaccion frenica en ginecologica. *Semana med Buoenos Aires* 1920; **27**: 243–8.
2. Curtis H. A cause of adhesions in the right upper quadrant in women. *J Am Med Ass* 1930; **98**: 1221–2.
3. Fitz-Hugh T Jr. Acute gonococcic peritonitis of the right upper quadrant in women. *J Am Med Ass* 1934; **102**: 2094–6.
4. Muller-Schoop JW, Wang SP, Munzinger J *et al. Chlamydia trachonitis* as a possible cause of peritonitis and perihepatitis in young women. *Br Med J* 1978; **1**: 1022–4.
5. Wolner-Hanssen P, Westrom L, Mardh PA. Perihepatitis and *Chlamydial salpingitis*. *Lancet* 1980; **i**: 901–3.
6. Paavonen J, Valtonen VV. *Chlamydia trachomatis* as a possible cause of peritonitis and perihepatitis in a young woman. *Br J Vener Dis* 1980; **56**: 341–3.
7. Darougar S, Forsey T, Wood JJ, Bolton JP, Allan A. Chlamydia and the Curtis–Fitz-Hugh syndrome. *Br J Vener Dis* 1981; **57**: 391–4.
8. Kimball MW, Knee S. Gonococcal perihepatitis in a male. *New Engl J Med* 1970; **282**: 1082–83.
9. Husebo OS, Bjerkesett T, Galland RB. *Act Chir Scand* 1979; **145**: 483–5.

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Case report

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Strangulating small bowel obstruction due to an intra-uterine contraceptive device

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The intra-uterine device is a common form of contraception particularly in parous women. It has a number of complications, which include pelvic infection, expulsion, dysmenorrhoea and menorrhagia[1,2]. Less commonly, perforation of the uterus may occur[3]. The present case report describes an unusual complication of uterine perforation by an intra-uterine contraceptive device (IUCD).

Case report

A 35-year-old woman was admitted with a 6 h history of constant lower abdominal pain of sudden onset, vomiting and diarrhoea. Her last menstrual period was 14 days before admission. An IUCD had been *in situ* for 5 years.

On initial examination, her blood pressure and pulse were normal and there was minimal lower abdominal tenderness. Bowel sounds were normal. Rectal examination was unremarkable but on vaginal examination the coil cord was not palpable. Investigations showed a mild leucocytosis but other investigations, including haemoglobin estimation, blood urea and electrolytes, blood glucose and serum amylase, were normal. Plain abdominal X-ray was of poor quality but a double loop coil was just visible in the pelvis. Fourteen hours after admission, the patient developed increasing abdominal pain. Re-examination revealed tenderness and guarding in the lower abdomen associated with absent bowel sounds.

At laparotomy the uterus was perforated by one limb of a sat-T-coil, (sometimes called double Lippes loop) which was adherent to the superior leaf of the small bowel mesentery. There was a loop of terminal ileum between the coil and small bowel mesentery. Six inches of terminal ileum was resected as it was non-viable and an end-to-end anastomosis was performed. The uterus was repaired and the other half of the coil was removed per vaginum. The patient made an uneventful postoperative recovery and was discharged on the seventh postoperative day.

Discussion

The reported incidence of uterine perforation from an IUCD is variable but for loop devices has been reported to occur in between 1 in 1000 and 1 in 2500 insertions[1,2].

Although most perforations are thought to occur at the time of insertion, the continued presence of the IUCD outside the uterine cavity is usually asymptomatic[2]. By contrast, in a small proportion of patients the abnormally situated IUCD may involve neighbouring viscera and produce a variety of clinical problems. Zakin *et al.*[4], in a review of 356 case studies of complete and partial uterine perforation, noted involvement of the gastrointestinal tract in 41 patients. Seventeen of these had developed small bowel obstruction due to herniation through a closed loop, strangulation by the IUCD string, volvulus around the IUCD or adhesions. The present patient provides, to our knowledge, the first report of strangulating small bowel obstruction due to a double loop which had partially perforated the uterus.

The diagnosis of complete or partial uterine perforation by an IUCD may be established by a combination of plain abdominal X-ray, ultrasonography, or hysterosalpingography. Eisenberg *et al.*[5] reported four cases of uterine perforation caused by a loop coil and described a characteristic widening of the loop on plain abdominal X-ray. This sign was present in our patient but its significance was not appreciated pre-operatively.

In conclusion acute abdominal symptoms and signs in young women with an IUCD should alert the clinician to the possibility of uterine perforation with its attendant complications.

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References

1. Hall RE. Comparative evaluation of intrauterine contraceptive devices. *Am J Obstet Gynecol* 1966; **94**: 65–71.
2. Nagel TC. Intrauterine contraceptive devices, complications associated with their use. *Postgrad Med J* 1983; **73**: 155–63.
3. Heartwell SF, Schlesselman S. Risk of uterine perforation among users of intrauterine devices. *Obstet Gynecol* 1983; **61**: 31–6.
4. Zakin D, Stern WZ, Rosenblatt R. Complete and partial uterus perforation and embedding following insertion of intrauterine device. *Obstet Gynecol Survey* 1981; **36**: 353–1.
5. Eisenberg RL. The widened loop sign of Lippes loop perforation. *Am J Radiol* 1972; **116**: 847–57.

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Peritoneal closure after lateral paramedian incision

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The lateral paramedian incision has been advocated as the strongest incision for abdominal surgery. We have evaluated this incision and tested the necessity for closing the deep peritoneal layer by a prospective randomized trial. All 206 patients undergoing laparotomy in the Surgical Unit in 1984, both elective and emergency cases, were included. In patients undergoing laparotomy through unscarred tissue, a lateral paramedian incision was performed and they were randomized to have either the peritoneum closed ($n=77$) *or left open* ($n=75$). *Patients in whom the laparotomy was performed through a previous incision* ($n=51$) *and those in whom the abdomen had to be opened urgently* ($n=3$) *were excluded from the trial but studied separately* ($n=54$). *The rectus sheath was closed with monofilament nylon in all cases. Patients were assessed for wound integrity during the immediate postoperative period and at 1, 3, 6 and 12 months after operation. So far the patients have been followed up for between 1 and 2 years and follow-up is continuing as in some cases incisional hernia may not be detected until several years after operation. There have been no cases of burst abdomen. No incisional hernias have developed in patients in whom a lateral paramedian incision was performed and the peritoneum was closed, and one incisional hernia has occurred in the patients in whom the peritoneum was left open. Seven incisional hernias have occurred in patients excluded from the trial of the lateral paramedian incision (13 per cent). We conclude that the lateral paramedian incision successfully abolishes the burst abdomen and that incisional hernia is rare. It is not necessary to close the peritoneum with this incision.*

Keywords: Lateral paramedian incision, peritoneum, incisional hernia

The lateral paramedian incision has been advocated for abdominal surgery because of its intrinsic strength[1,2]. The incision is performed more laterally than a conventional paramedian incision; the rectus sheath is incised at the junction of the outer and middle thirds of the width of the sheath. The peritoneum is incised in the same line as the rectus sheath and the wound is said to be inherently strong due to the wide shutter mechanism that is produced. In closing this incision its innovators employ a layer of sutures in the peritoneum and a second layer in the rectus sheath. In this study we have examined the necessity for closing the peritoneum, for it has been shown for conventional vertical abdominal incisions that closure of the peritoneum is unnecessary[3].

Patients in whom a laparotomy was performed through a previous incision were excluded from the trial of the lateral paramedian incision and have been studied as a separate group, for they also present difficulties with wound healing, as the incision is made through pre-existing scar tissue.

Patients and methods

All patients undergoing laparotomy (both elective and emergency) on the Surgical Unit during the year 1984 were included ($n=206$). In 152 patients, the laparotomy was performed through unscarred tissue using a lateral paramedian incision (Group I). This was performed as previously described[1,2,4] by incising the rectus sheath at the junction of its outer and middle thirds. The rectus muscle was then dissected out and retracted laterally and the inner rectus sheath and peritoneum were incised in the same line as the outer sheath. The incision was angled towards the xiphisternum or pubic symphysis for operations at the upper and lower extremities of the abdomen.

Patients were randomized into two groups for closure of the wound by a random allocation held by a third party. In the first group the abdominal wall layers deep to the rectus muscle were left open ($n=75$) and in the second group these layers were closed with No. 1 chromic catgut ($n=77$). In all patients the anterior sheath was closed with No. 1 monofilament nylon mounted as a loop on a 7/8 Moynihan-type hand needle. Sutures were placed at least 1 cm from the wound edge and at intervals no greater than 1 cm.

Patients in whom the laparotomy was performed through the scar tissue of a previous abdominal operation were excluded from the trial of the lateral paramedian incision ($n=51$) as were patients in whom urgency precluded the necessary dissection ($n=3$). These patients were studied as a separate group (Group II, $n=54$). In patients in whom the operation was performed through a previous scar, the wound was closed with No. 1 monofilament nylon using a mass closure technique. This incorporated all layers of the wound except the skin with each stitch. No tension sutures were used and the subcutaneous fat was not sutured. Peritoneal drains were placed through separate stab incisions and no wound drains were used.

The wounds of all patients were examined daily during the immediate postoperative period and then at 1, 3, 6 and 12 months after operation. The type of closure was not masked from the assessors. Infection, sinus formation and herniation were recorded. Incisional hernia was defined as a defect in the scar which could be detected by clinical examination. The clinical examination routinely included tensing of the abdominal muscles to facilitate such detection and this was achieved by asking the patient to raise first the head and then the legs up off the examination couch. Patients have been followed up for between one and two years following operation.

In patients going abroad, follow-up has been by correspondence

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with the patient and doctor. Patients that died during the follow-up period were considered to have completed their follow-up for the purposes of the 'completeness of follow-up' results. Only those who defaulted from follow-up or who were abroad and not able to be contacted were considered as 'lost to follow-up'.

Results

The results of the trial are shown in *Table 1*. Burst abdomen did not occur in any patient. A single incisional hernia has occurred to date in a lateral paramedian incision (Group I) in which the deep layers were left open. This patient underwent laparotomy for an aortic aneurysm and eight months later disseminated carcinoma of the lung was diagnosed. The incisional hernia appeared one year after the original operation, by which time the patient had disseminated bony metastases and had lost weight. Incisional hernia was more common in Group II in patients in whom a previous scar was re-opened. The incisions through which the operations were performed are shown in *Table 2* and it can be seen that some of these incisions were being opened for the fourth time.

Follow-up was generally good in this trial and was incomplete at one year in only 27 patients (13 per cent). Ten of these patients defaulted because they returned to their home countries. Completeness of follow-up is shown in *Table 3*.

Table 1 *Results*

	Group I		
	Peritoneum closed	Peritoneum open	Group II
Number	75	77	54
Burst abdomen	0	0	0
Superficial dehiscence (skin only)	1	0	0
Wound infection	7	9	7
Incisional hernia	0	1	7
Sinus formation	2	1	1
Died during follow-up	14	13	12
Defaulted during follow-up	9	9	9
Second operation during follow-up	1	1	0

Discussion

This study has confirmed the findings of Donaldson *et al.*[1] and Guillou *et al.*[2] that the lateral paramedian incision has certain excellent properties. It has great intrinsic strength in the immediate postoperative period to the extent that burst abdomen did not occur. Its strength seems to persist into the later stages of wound healing as incisional hernia has only occurred in a single patient so far. This last figure is encouraging but is only provisional as incisional hernias may become apparent many years after operation[5–8].

The strength of the lateral paramedian incision has been attributed to the formation of a shutter mechanism[1,4]. When the incision is sutured after laparotomy, the suture lines are

Table 3 *Completeness of follow-up*

	Patients seen		
	Group I		
Months after operation	Peritoneum closed $n=75$ (%)	Peritoneum open $n=77$ (%)	Group II $n=54$ (%)
1	73/75 (97)	77/77 (100)	50/54 (93)
3	73/75 (97)	77/77 (100)	50/54 (93)
6	72/75 (96)	74/77 (96)	50/54 (93)
12	66/75 (88)	68/77 (88)	45/54 (83)

Table 2 *Incisional herniae* (*Group II*)

Patient number	Incision	Length × depth (cm)	Hernia found (months after operation)	Operations performed
5	R P/M	26 × 3	6	1 Cholecystectomy 2 Choledochojejunostomy 3 *Refashioning of choledochojejunostomy
6	M/L	21 × 3	11	1 Cholecystectomy + fundoplication 2 Incisional hernia repair 3 Incisional hernia repair 4 *Strangulated incisional hernia
19	M/L	25 × 3	11	1 Laparotomy for rectal bleeding 2 R.hemicolectomy 3 *Ileorectal anastomosis for angiodysplasia
21	M/L	19 × 3	4	1 Hysterectomy 2 *Ovarian cystectomy for carcinoma N.B. postoperative radiotherapy
22	R P/M	28 × 2	7	1 Nephrolithotomy 2 Nephrectomy 3 Incisional hernia repair 4* Incisional hernia repair
30	M/L	18 × 3	10	1 Hysterectomy 2 *Ovarian cystectomy for fibrothecoma
50	R S/C	21 × 2·5	11	1 Cholecystectomy 2 *Choledochoduodenostomy

Key: R P/M, right paramedian; M/L, midline; R S/C, right subcostal; *, current operation protected from centripetal forces by their position in relation to the rectus muscle. This present trial supports the theory of the shutter mechanism, for in half of our patients the layers deep to the rectus were not sutured and the integrity of the wound depended on the anterior sheath only and the anatomical configuration of this shutter. However, we do not feel that the shutter arrangement is sufficient in itself but merely contributes to wound strength for closure of the anterior sheath is essential. We used a non-absorbable suture for this, although the originators of the incision used absorbable sutures. It has previously been shown for the conventional paramedian incision that closure of the peritoneum is unnecessary[3].

The lateral paramedian incision does have certain disadvantages. It takes longer to perform than either midline or conventional paramedian incisions and the technique requires a period of time to be learnt. Its cosmetic appearance and the access it provides are different from conventional incisions but these become acceptable with familiarity. If a subsequent laparotomy is required after healing is complete, then, if the same incision is re-used, a second dissection of the rectus muscle is usually not possible and the rectus either has to be split or a fresh incision made in unscarred tissue.

The patients in this study who were excluded from the trial of the lateral paramedian incision are an interesting group with quite different problems. In all these patients, except three whose abdomens had to be opened urgently, the laparotomy was performed by re-opening the scar of a previous laparotomy. Although many studies have been performed on the relative merits of different incisions made in unscarred tissue, there is a paucity of information relating to the healing of incisions through existing scars, although this is obviously a much more difficult group. In these patients (Group II) burst abdomen also did not occur and we attribute this to the technique of suturing which specified large bites of tissue, for which purpose the Moynihan hand-held 7/8 needle is essential. Although wound integrity was satisfactory in the immediate postoperative period, later healing was less satisfactory, as shown by the development of incisional hernia in seven of the 54 patients in this group (13 per cent). The healing of scar tissue is therefore less sound than freshly incised tissues and more research is necessary to determine the best technique for the closure of such wounds.

References

1. Donaldson DR, Hegarty JH, Brennan TG, Guillou PJ, Finan PJ, Hall TJ. The lateral paramedian incision – experience with 850 cases. *Br J Surg* 1982; **69**: 630–32.
2. Guillou PJ, Hall TJ, Donaldson DR, Broughton AC, Brennan TG. Vertical abdominal incisions – a choice? *Br J Surg* 1980; **67**: 395–99.
3. Ellis H, Heddle R. Does the peritoneum need to be closed at laparotomy? *Br J Surg* 1977; **64**: 733–36.
4. Ellis H, Bucknall TE, Cox PJ. Abdominal incisions and their closure. *Current Problems in Surgery* 1985; **22**: 5–51.
5. Harding KG, Mudge M, Leinster SJ, Hughes LE. Late development of incisional hernia: an unrecognised problem. *Br Med J* 1983; **286**: 519–20.
6. Ellis H, Gajraj H, George CD. Incisional hernias: when do they occur? *Br J Surg* 1983; **70**: 290–91.
7. Ausobsky JR, Evans M, Pollock AV. Does mass closure of midline laparotomies stand the test of time? A random control clinical trial. *Ann R Coll Surg Engl* 1985; **67**: 159–61.
8. Mudge M, Hughes LE. Incisional hernia: a 10 year prospective study of incidence and attitudes. *Br J Surg* 1985; **72**: 70–71.

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Pancreatic resection for carcinoma of the pancreas and the periampullary region in patients over 70 years of age

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This study was undertaken to elucidate whether or not resection for cancer of the pancreas and the periampullary region can be performed with an acceptable survival rate in patients over 70 years of age ($n=21$) as compared with patients under 70 years of age ($n=47$), and whether resection provides an improvement in their prognosis and longevity. The operative mortality for patients over 70 years of age and under 70 years was 10 and 9 per cent respectively and the cumulative 5 year survival 12 ± 11 and 20 ± 9 per cent respectively. The median survival was 11 months in both groups. It was concluded that an age of 70 years or more is not an absolute contra-indication for pancreatic resection. Prognosis is related to tumour histology.

Keywords: Pancreatic neoplasm; pancreatic resection; geriatric surgery

The incidence of cancer of the pancreas and the periampullary region is increasing[1], but the patients are often elderly, approximately 80 per cent of cases occurring between the ages of 60 and 80 years[2]. Most authors emphasize that there is rarely any justification for performing major resection in a patient over 70 years of age owing to a prohibitively high mortality and morbidity and a short survival time[3–6]. A preliminary study suggested that age as such is not a limiting factor for resection[7], as has also been pointed out in gastric and colorectal surgery[8,9]. This encouraged the authors to continue an aggressive policy regarding the treatment of carcinoma of the pancreas and the periampullary region in patients aged 70 years or older.

The purpose of this survey was to evaluate whether or not the indications for pancreatic resection must still encompass the surgical risk of an aged person as a special entity and, if resection can be performed with an acceptable survival rate in the elderly, whether there is any real improvement in their prognosis and longevity.

Patients and methods

During the years 1968–1985, 327 patients were treated for carcinoma of the pancreas and the periampullary region at the Oulu University Central Hospital. Sixty-eight of these (21 per cent) underwent resection, 164 (50 per cent) a palliative bypass procedure and 57 (17 per cent) laparotomy and biopsy, while 38 (12 per cent) were treated non-operatively. Twenty-one of the patients undergoing pancreatic resection (31 per cent) were 70 years of age or older and 47 (69 per cent) under 70 years of age. A comparison of the groups and types of resection is presented in *Tables 1* and *2*.

The retrospective survey of the results of treating pancreatic and periampullary cancer in 1981 suggested that age as such is not a limiting factor for pancreatic resection, and thus all patients with a resectable tumour who were fit for operation, regardless of age, were prospectively subjected to pancreatic resection from 1982 onwards.

During the earlier years, 1968–1976, the overall operative mortality rate for pancreatic resection was 36 per cent, the figure being 25 per cent for patients ≥70 years old and 43 per cent for those <70 years old. After that date the operative technique was standardized and the operation was performed continuously by the same surgeons[7]. During the latter period, 1977–1985, the overall operative mortality rate decreased to 4 per cent, 6 per cent for patients ≥70 years old and 3 per cent for patients <70 years old. There were no operative deaths, i.e. deaths occurring within 30 days of surgery or during the same hospitalization, in patients <70 years old during the last 5 year period 1981–1985.

All patients were followed up until 31 December 1985 or their death. Seven (33 per cent) of the patients aged ≥70 years and 15 (32 per cent) of those aged <70 years were alive at the end of the observation period.

Table 1 *Comparison of the groups*

	No. of patients	M/F (%)	Age (years) mean ± s.d.	Adeno-carcinoma of the pancreas (%)	Radical resection (%)
≥ 70 years	21	57/43	74 ± 3	62	71
< 70 years	47	38/62	58 ± 9	55	68
Total	68	44/56	64 ± 11	56	69

Table 2 *Types of pancreatic surgery performed*

	Total		Whipple		Distal		Local	
Age	No.	(%)	No.	(%)	No.	(%)	No.	(%)
≥70 years	1	(5)	15	(71)	4	(19)	1	(5)
<70 years	7	(15)	36	(77)	4	(9)	—	
Total	8		51		8		1	

After the exclusion of operative mortality, the life-table method[10] was used to analyse survival and the Mantel–Haenszel χ^2 test[11] for statistical evaluation. A P value of <0·05 was chosen as the level of confidence.

Results

Two (10 per cent) of the patients aged ≥70 years and 4 (9 per cent) of those aged <70 years died. Of the patients aged ≥70 years, one died of myocardial infarction and the other of congestive heart failure. Two of the patients aged <70 years died of anastomotic leakage, one of intestinal perforation and one of myocardial infarction. All postoperative deaths followed Whipple's operation.

Analysis of the postoperative complications is presented in *Table 3*. Anastomotic leakage was the most common complication. Two of the three leaks from pancreatic anastomosis proved to be fatal. All pancreatic leaks occurred in the patients aged <70 years. Chest and wound problems were not related to age. There was a complication in 10 patients (48 per cent) in the ≥70 age group, and 14 (30 per cent) in patients aged <70 years.

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The median survival in both groups was 11 months. The cumulative 5 year survival was somewhat lower in the patients aged ≥70 years, but not significantly so (*Figure 1*). All late deaths in the patients aged ≥70 years and all but two in the younger patients were due to recurrent cancer. Two patients aged <70 years died of myocardial infarction, one 5 months after total pancreatectomy and the other 16 months after Whipple's operation. No signs of recurrent cancer were detected at autopsy.

Survival as related to tumour histology is shown in *Table 4*. There were no significant differences between the groups. Of patients with periampullary carcinoma, those under the age of 70 fared better, but the difference was not significant. There were no 5 year survivors in the pancreatic carcinoma group, whereas the overall cumulative 5 year survival for periampullary cancer was 45±15 per cent.

Table 4 *Survival in relation to tumour histology*

Age	No. of patients	Mean ±s.d. (months)	Range (months)	Median (months)	Cumulative 5-year survival ±s.d. (%)
Adenocarcinoma of the pancreas					
≥70 years	11	11±12	1–44	9	—
<70 years	24	11±10	1–44	8	—
Overall	35	11±11	1–44	9	—
Periampullary carcinoma					
≥70 years	8	25±24	>10 years	20	25±22 } n.s.
<70 years	19	43±40	>10 years	36	58±19 }
Overall	27	34±32	>10 years	28	45±15

n.s., not significant

Discussion

The relative and absolute numbers of elderly patients in Western societies continue to increase, as does the incidence of pancreatic cancer. It is generally held that geriatric patients do not fare as well as their contemporaries after pancreatic resection[4–6], and it has been suggested, but not yet clearly demonstrated, that there is no improvement in their prognosis or longevity after resection[3]. Pancreatic resection nevertheless offers the only hope for long-term survival, or at the least comfortable palliation. Before we deny our aged patients this possibility, the role of age as a factor in operative mortality and longevity must be seriously investigated.

Table 3 *Postoperative complications*

Complication	No. of complications Overall	 Patients ≥70 years of age
Anastomotic leakage	9	4
Pancreatic	3	—
Biliary	6	4
Intra-abdominal abscess	5	1
Postoperative pancreatitis	3	1
Cardiac	3	2
Myocardial infarction	2	1
Congestive heart failure	—	1
Pulmonary	2	1
Pneumonia	—	1
Pulmonary emboly	1	—
Wound infection	2	1
Postoperative bleeding	1	—
Renal failure	1	—

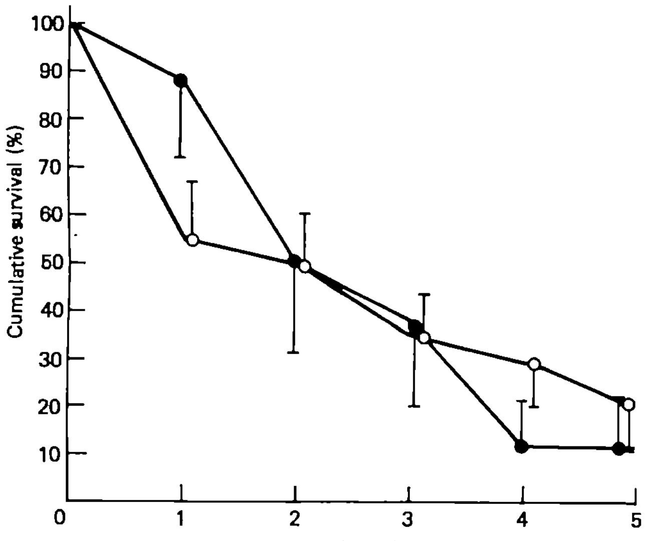

Figure 1 *Cumulative survival after pancreatic resection in patients ≥70 (●) and <70 years (○) of age*

The mortality of 10 per cent for patients aged 70 or older in the present study was of approximately the same magnitude as that reported recently after colon surgery[8] and total gastrectomy[9] in the elderly, but markedly lower than the 20–33 per cent for pancreatic resection, also reported earlier[4,5]. Bittner *et al.*[9] emphasize that operative death associated with major surgical procedures has decreased significantly in elderly patients during recent years. Mortality rate after total gastrectomy was 3·6 per cent for patients under 70 years of age and 4·4 per cent for patients over 70 years. By comparison, the mortality rate for pancreatic resection during the latter period, studied here from 1977 to 1985, was 3 per cent in patients under 70 years of age and 6 per cent in those over 70 years. Hence pancreatic resection for cancer in the elderly can be performed at present with an acceptable mortality, which according to Trede[12] is approximately 5 per cent or less. Only a mortality rate as low as this justifies pancreatic resection, even though it may result in palliation for only one or two years[6].

Forrest and Longmire[3] report that the average survival time for patients over 70 years of age after pancreatic resection is significantly worse than that for patients under 70 years of age, coming close to that for patients undergoing a palliative bypass procedure. Statistically, there seemed to be no justification for performing major pancreatic resection in a patient over 70 in preference to a simple bypass. The same authors recommend that very careful selection should be made before a Whipple operation is performed in a patient of this age. In the present study the median and cumulative survival rates were similar in both groups, although patients with periampullary cancer who were under 70 fared somewhat better. The median survival time after resection was twice as long as that reported after palliative bypass[7]. Long-term results and longevity were mostly related to tumour histology.

Resection offers the only hope for long-term survival in patients with pancreatic and periampullary cancer. The decision to operate is often confused by the effects of ageing. The present results indicate that the patient's physiological age and not his chronological age is crucial when evaluating his eligibility for resection, and suggest that resection improves the long-term prognosis and quality of life regardless of the patient's age.

We conclude that age as such is not a limiting factor for pancreatic resection. Resection can be performed with an acceptable survival rate even in patients over 70 years of age if enough attention is drawn to careful patient selection and proper preparation. The long-term prognosis is nevertheless related to tumour histology.

References

1. Levin DL, Conelly RR, Devesa SS. Demographic characteristics of cancer of the pancreas: mortality, incidence and survival. *Cancer* 1981; **47:** 1456–68.
2. Cordis L, Cold EB. Epidemiology of pancreatic cancer. *World J Surg* 1984; **8:** 808–21.
3. Forrest JF, Longmire WP. Carcinoma of the pancreas and periampullary region. A study of 279 patients. *Ann Surg* 1979; **189:** 129–38.
4. Herter FP, Cooperman AM, Ahlborn TN, Antinore C. Surgical experience with pancreatic and periampullary cancer. *Ann Surg* 1982; **195:** 274–81.
5. Obertop H, Bruining HA, Eetinck Schattenkerk M, Eggink WF, Jeekel J, van Houten H. Operative approach to cancer of the head of the pancreas and the periampullary region. *Br J Surg* 1982; **69:** 573–76.
6. Piorkowski RJ, Blievernicht SW, Lawrence Jr WL, Horsley III JS, Neifeld JP, Terz JJ. Pancreatic and periampullary carcinoma. Experience with 200 patients over a 12 year period. *Am J Surg* 1982; **143:** 189–93.
7. Kairaluoma MI, Partio E, Ståhlberg M, Laitinen S. Pancreatic and periampullary carcinoma. *Ann Chir Gynaecol* 1984; **73:** 199–205.
8. Greenburg AG, Salk RP, Pridham D. Influence of age on mortality of colon surgery. *Am J Surg* 1985; **150:** 65–70.
9. Bittner R, Schirrow H, Butters M, Roscher R, Krautzberger W, Oettinger W, Beger HG. Total gastrectomy. A 15-year experience with particular reference to the patient over 70 years of age. *Arch Surg* 1985; **120:** 1120–25.
10. Cutler SJ, Ederer F. Maximum utilization of the life table method in analysing survival. *J Chron Dis* 1958; **8:** 699–712.
11. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959; **22:** 719–48.
12. Trede M. The surgical treatment of pancreatic carcinoma. *Surgery* 1985; **97:** 28–35.

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Surgical staging of gastric carcinoma: sources and consequences of error

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Macroscopic 'TNM' staging was performed during 78 consecutive operations for gastric carcinoma and compared with subsequent pathological staging. Surgical assessment was correct for tumour (T) in 60 per cent when depth of invasion was assessed, for nodes (N) in 61 per cent, for liver metastases (M) in 92 per cent but for all aspects in only 21 per cent. Curability (conservatively defined as T_{1-3}, N_{0-1}, M_0) was correct in 8 of 18 patients thus assessed at surgery and incurability was pathologically correct in 58 of 60 patients. Despite inaccurate surgical staging, no patient was denied a resection although 10 patients had unduly radical procedures for their stage and 2 had inappropriately conservative procedures for their stage (but without evidence of residual disease). Staging errors did not jeopardize conventional surgical management substantially and use of intra-operative microscopic sampling of nodes would have improved surgical treatment only minimally.

Keywords: Gastric neoplasms, staging

Surgeons decide which operation to perform for a patient with gastric carcinoma on the basis of their intra-operative estimate of the extent of the tumour. Morbidity and survival differ after resection for cure, resection for palliation, a bypass procedure for relief of obstruction and laparotomy alone; consequently it is important that each patient should undergo an operation appropriate to the stage of the tumour. The aim of this study was to establish the accuracy with which a surgeon could stage disease intra-operatively using macroscopic assessment alone, and how correctly he could separate curable from incurable disease. We also determined whether accurate staging was needed to select an appropriate operation.

Methods

Seventy-eight consecutive patients with a pre-operative diagnosis of gastric carcinoma who underwent laparotomy were studied prospectively. The operative staging was performed by two surgeons using the UICC TNM staging system[1], and a pathologist subsequently staged the pathological material for comparison (*Table 1*). The clinical TNM system is essentially identical to the pathological TNM in N and M assessment but differs in T assessment: the clinical T stage is assessed from the presence or absence of 'deep involvement' and the geographical extent of regional involvement, whereas the pathological T stage depends on depth of invasion alone. For the purpose of this study we therefore used a macroscopic assessment of depth identical to the pathological T stage to allow comparison. T_1 lesions were diagnosed when the lesion felt mobile on the muscle layer of the stomach wall, T_2 when it was fixed to muscle, T_3 when serosal involvement was visible and T_4 when the lesion adhered to an adjacent viscus. Nodes were considered involved if enlarged or hard, and the M stage was assessed from lesions seen or palpated in the liver or omentum. The pathologist assessed the T stage in the resected specimen, or from a biopsy of the site of maximal serosal involvement or of an adjacent involved organ; the N stage was assessed by sampling of the N_1 nodes (resected or biopsied nodes within 3 cm of the tumour) and N_2 nodes were examined by biopsy of the coeliac and common hepatic artery nodes, thereby sampling 'worst case' N_2 nodes away from the gastric wall. N_3 nodes were also sampled where feasible (usually the hepatoduodenal node) but this was not always possible. The M stage was assessed by biopsy of liver metastases or a wedge of the most abnormal part of the liver, as well as from the resected omentum or a biopsy of the most abnormal part. Peritoneal fluid or washings from the tumour area were examined cytologically.

The surgeon also decided intra-operatively whether the patient was curable or incurable. For the purpose of this study we used T_{1-3} N_{0-1} M_0 as a definition of curability. We chose this watershed because adjacent organ involvement (T_4 disease)[2], involvement of nodes at a distance from the stomach along the coeliac or common hepatic artery[3], or the presence of metastases[2] all confer a substantially worse prognosis.

We finally assessed whether the surgery had been appropriate or not. Our policy was to perform a conventional radical gastrectomy[4,5] for 'curable' carcinoma as we defined it; this involved transecting the stomach 5 cm clear of macroscopic tumour without frozen section confirmation, omentectomy, removal of 3 cm of duodenum with the nodes adjacent to the right gastric artery and ligation of the left gastric artery at its origin with removal of nodes contained in the pedicle. If categorized by the Japanese system[6] this procedure would probably fall between an 'R_1' and an 'R_2' resection. Four patients from a parallel study are included who had a formal R_2 lymphadenectomy of the common hepatic, splenic and retropancreatic nodes with removal of the superior leaf of mesocolon and pre-pancreatic peritoneum; they were also staged by surgeon and pathologist according to our protocol. Cases judged to be incurable had a gastrectomy without node clearance, or a gastroenterostomy if an obstructing distal carcinoma was not resectable. When resection appeared technically unsafe and there was no clinical or radiological evidence of gastric outlet obstruction, laparotomy alone was performed.

Table 1 *UICC pathological TNM system*[1]

Primary tumour	
T_{is}	Pre-invasive carcinoma
T_0	No histological carcinoma
T_1	Mucosa or submucosa invaded
T_2	Muscularis propria or subserosa invaded
T_3	Serosa invaded
T_4	Contiguous structures invaded
Lymph nodes	
N_0	No nodes involved
N_1	Involved nodes within 3 cm of tumour along lesser or greater curvature
N_2	Involved nodes over 3 cm from tumour including nodes along left gastric, splenic coeliac and common hepatic arteries
N_3	Involved para-aortic, hepato-duodenal or other intra-abdominal nodes
Metastases	
M_0	No distant metastases
M_1	Distant metastases

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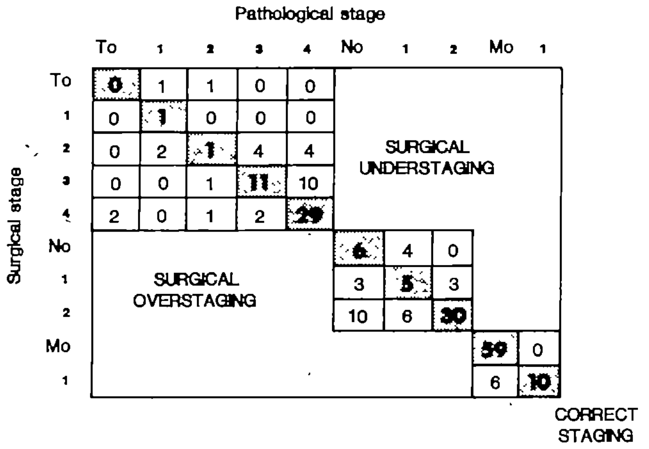

	To	1	2	3	4	No	1	2	Mo	1
To	0	1	1	0	0					
1	0	1	0	0	0					
2	0	2	1	4	4					
3	0	0	1	11	10					
4	2	0	1	2	29					
No						6	4	0		
1						3	5	3		
2						10	6	30		
Mo									59	0
1									6	10

Figure 1 *Comparison between surgical and pathological staging indicating surgical overstaging, understaging and (shaded) correct staging in 70 patients (T), 67 patients (N) and 75 patients (liver M). The N_2 level was represented by coeliac and common hepatic artery nodes*

Results

Errors in staging: extent and causes (Figure 1)

The pathological T stage was assessed in 70 patients in whom the pathologist found the material adequate for accurate staging. Two cases had been categorized by the surgeon as T_0 (no carcinoma palpable), one as T_1, eleven as T_2, twenty-two as T_3 and thirty-four as T_4. Staging had been correct in 42 patients (60 per cent), overstaging had occurred in 8 (11 per cent) and understaging in 20 (29 per cent). The overstaging errors were due to two T_1 lesions diagnosed as T_2, the incorrect diagnosis of serosal invasion in a T_2 case and five cases where invasion of an adjacent organ was not confirmed by the pathologist in tissue which the surgeon expected to confirm T_4 spread. The understaging errors were due to the underestimation of omental spread (14 cases) or serosal involvement (4 cases) and to two biopsy-proven but surgically impalpable tumours. In the two patients with impalpable neoplasms histology revealed a T_1 and a T_2 carcinoma.

The pathological N stage could be determined in 67 patients: 10 were staged by the surgeon as N_0, 11 as N_1 and 46 as N_2. The intra-operative stage had been correct in 41 patients (61 per cent) but was overestimated in 19 patients (28 per cent) and underestimated in 7 (11 per cent). In the 19 patients in whom the surgeon overstaged nodal disease, the pathologist found that 15 had reactive nodes, 2 had features of granulomatous inflammation and in 2 the surgeon had submitted normal pancreatic tissue as involved nodes.

Metastatic spread was assessed in the liver, omentum (at a site not contiguous with the tumour) and in the peritoneal fluid. Ten of the seventy-five liver biopsies showed histological metastases and all had been identified by the surgeon. While within the limitations of our operative assessment there were no missed metastases, six cases (8 per cent) had metastases incorrectly diagnosed. Histologically these showed non-specific inflammation (two cases), bile duct hamartomas, a calcified haemangioma, fatty change and normal liver tissue. Of the 75 liver biopsies, 92 per cent were thus correctly staged and 8 per cent overstaged. Distant metastases to the omentum were diagnosed at operation in 16 patients but only 11 were confirmed histologically (69 per cent) while the remaining five (31 per cent) had histological findings of tumour-free lymph nodes (two), fibrous tissue, lymphoid aggregates and normal omentum. Peritoneal fluid cytology was positive in 5/51 patients in whom 3 had metastases and 2 advanced serosal disease. The surgeon predicted incurability from the TNM stage in four of the five patients but failed to recognize extensive serosal involvement in the remaining case.

Overall, 67 cases yielded enough material to correlate full surgical TNM staging with pathological staging. There was complete agreement about T, N and M stage in only 14 patients (21 per cent).

Accuracy in assessing curability and selecting appropriate operations

Using our definition of curability the surgeon staged 18 patients as having curable and 60 as having incurable disease. The pathologist confirmed curability in only 8/18 patients (44 per cent) (*Table 2*) and confirmed incurability in 58/60 patients (97 per cent). The ten incorrect assessments in the clinically 'curable' group were due to omental involvement in seven cases (of whom three had proximal resection line disease), isolated proximal resection line disease, a metastasis to a hepatic artery node in one patient and malignant cells in peritoneal washings in another. The two wrong assessments in the clinically incurable group were as follows. The first was in a patient staged at operation as T_2 N_3 because of grossly enlarged mesenteric and para-aortic nodes which were shown to be reactive, the pathological stage being T_1 N_0. In another patient clinically staged as T_4 N_3 M_1 no carcinoma was found in the gastrectomy specimen, although it included the site of a healed perforation at which a previous operative biopsy had revealed an invasive gastric carcinoma, which was confirmed on histological review.

Our final assessment was whether the patient had undergone an appropriate operation, and whether inappropriate operations adversely influenced the likelihood of cure and operative morbidity (*Table 3*). Sixty-six of the seventy-eight patients (85 per cent) had procedures appropriate to our policy. Ten (13 per cent) were incorrectly assessed as curable and had, according to our protocol, inappropriately radical procedures (including four R_2 lymphadenectomies). The pathologist defined seven of the ten as incurable because of omental invasion and one each because of resection line disease, common hepatic node involvement and positive peritoneal cytology. It is likely that some cases of omental invasion had all disease encompassed by the resection. A wrong surgical assessment of incurability was made in two patients owing to extensive non-malignant lymphadenopathy or adhesions. While both had conventional gastrectomies (and should have had radical gastrectomies according to our protocol) histological assessment suggested both tumours had been completely removed. Thus while 12 patients were incorrectly assessed, all underwent resection of the carcinoma, but according to our protocol in 10 this was inappropriately radical and in 2 inappropriately conservative.

Table 2 *Pathologist's assessment of curability in 18 patients deemed surgically curable*

Curable		Incurable	
Surgeon	Pathologist	Surgeon	Pathologist
$T_0N_0M_0$	$T_1N_0M_0$	$T_2N_0M_0$	$T_3N_1M_0$*
$T_0N_0M_0$	$T_2N_0M_0$	$T_2N_0M_0$	$T_4N_0M_0$
$T_1N_0M_0$	$T_1N_1M_0$	$T_2N_1M_0$	$T_3N_2M_0$
$T_2N_0M_0$	$T_1N_0M_0$	$T_2N_1M_0$	$T_4N_2M_0$*
$T_2N_0M_0$	$T_3N_1M_0$	$T_2N_1M_0$	$T_4N_0M_0$
$T_2N_1M_0$	$T_2N_0M_0$	$T_2N_1M_0$	$T_4N_1M_0$
$T_2N_1M_0$	$T_3N_0M_0$	$T_3N_1M_0$	$T_4N_1M_0$
$T_3N_0M_0$	$T_2N_0M_0$	$T_3N_1M_0$	$T_4N_2M_0$*
		$T_3N_1M_0$	$T_3N_1M_1$†
		$T_3N_1M_0$	$T_4N_1M_0$*

*Resection line involvement; † positive peritoneal cytology

Table 3 *Correctness of surgical procedures*

	Correct (%)	Incorrect	Total
Laparotomy only	16 (100)	0	16
Gastroenterostomy	10 (100)	0	10
Palliative gastrectomy	32 (94)	2	34
Radical gastrectomy	8 (44)	10	18
Total	66	12	78

Mortality and morbidity

There were three deaths. Major morbidity occurred in four patients (delayed gastric emptying, subphrenic abscess, anastomotic leak, re-operation for anastomotic bleeding). Deaths and major morbidity were confined to the group which had appropriate surgery and no complications could be attributed to incorrect surgical staging.

Discussion

The accuracy with which gastric carcinoma is staged intra-operatively may be considered important because major therapeutic decisions depend on the extent of the disease. Overestimation may result in an unduly conservative operation and reduce the likelihood of cure, while underestimation may result in inappropriately radical surgery with its attendant risks. We have examined the problem at two levels: firstly we analysed the accuracy of macroscopic TNM staging and secondly we calculated whether it was important to stage accurately if the surgeon's philosophy favoured resection whenever technically possible.

At the first level, our attempt to perform macroscopic TNM staging was very inaccurate indeed, being correct in only 21 per cent of patients. We most often underestimated T stage and overestimated N and M stage.

We failed to reproduce the accurate surgical assessment of T stage (particularly of serosal and adjacent organ involvement) reported from Japan[3]. However, underestimated serosal spread and attempted staging of invisible or impalpable tumours had little influence on our therapeutic decisions. More important was unsuspected omental invasion (T_4), which caused most underestimation of T stage. While the UICC system[1] does not subdivide the T_4 category, the AJCC system[7] defines omental invasion as T_{4a}, including in this category invasion of the spleen and colon as well as 'intraluminal invasion' of the oesophagus or duodenum, which clearly have a poor prognosis. We suspect that omental invasion is an adverse prognostic feature but believe it should not preclude attempted cure, which would include omentectomy. However, accurate intra-operative histological assessment of omental invasion seems impossible, from our high sampling error in this study. We therefore conclude that intra-operative microscopic assessment of T stage will seldom be of benefit.

We incorrectly assessed the nodal status of 39 per cent of cases, usually suspecting metastases when palpating reactive nodes. In this we were also far less accurate than Japanese workers[3]. Microscopic intra-operative assessment of node spread has been reported by Kajitani using frozen section histology[8] and by Keighley's group, who compared the sensitivity of imprint cytology to that of frozen sections[9]. While either approach would provide the surgeon with a more accurate assessment of nodal spread, our data suggest that this information would seldom have helped select a more appropriate operation. Our macroscopic assessment of lymph nodes did not influence whether patients had a resection or not, but did influence the choice between a palliative or curative resection. Because of this only two patients would have benefited from intra-operative nodal histology, one having had an 'inappropriately' radical nodal clearance in the presence of common hepatic (N_2) involvement and the second an inappropriately conservative gastrectomy (according to our protocol) but without apparent disadvantage, as the pathologist judged the resection to be complete. Therefore more precise assessment of nodal status will rarely improve surgical strategy if a conventional radical gastrectomy is used for cure. If, on the other hand, our arbitrary placing of the boundary of curability was changed from the N_1/N_2 level (within 3 cm of tumour/common hepatic, coeliac) to the N_2/N_3 level (common hepatic, coeliac/hepatic, para-aortic) to allow radical lymphadenectomy then intra-operative microscopic examination of the N_3 tier might become important.

The frequency with which we misdiagnosed metastatic disease in both the liver and omentum was noteworthy. We probably underestimated the true incidence of metastases as we sampled only visible or palpable abnormalities and some patients may have had impalpable intrahepatic deposits. None the less, no patient was inappropriately denied a resection, as a result of our policy of removing the primary whenever this appeared technically safe. We suggest, however, that any apparent metastasis should be biopsied to provide an accurate prognosis.

Resection line disease is a common and ultimately lethal problem following 'curative' gastrectomy[10]. However, in three of our four cases there was also direct invasion of the omentum, so resection line tumour could simply have been a sign of associated incurable disease rather than its sole cause. It does not therefore follow that routine frozen section examination of the resection line would frequently improve the surgeon's ability to cure the patient. Moreover, complete sampling of the proximal resection line would arguably be too time-consuming to be performed intra-operatively because of the number of sections required.

An important question was whether any patient suffered as a result of inappropriate surgery and whether not using intra-operative cytological or histological assessment was a disadvantage. Our policy of resecting the primary tumour whenever this appeared technically safe meant that no patient was denied a gastrectomy. The debate therefore hinges on the extent of resection: whether a curable patient has less chance of survival following a 'palliative' resection and whether an incurable patient is disadvantaged by a 'radical' procedure. If the view (which we do not share) is that cure is only possible with nodal disease within 3 cm of the tumour (N_1) then conventional gastrectomy (Japanese R_1) would provide both palliation and cure and accurate intra-operative staging would be unimportant. If, however, involved nodes at a distance on the gastric wall still imply curable disease (N_1 and some N_2 nodes) then the traditional radical gastrectomy (more extensive than the Japanese R_1 but falling short of R_2) would remove all curable disease and intra-operative histology – as we have shown – would again have little value. If, however, it is believed that cure should be sought by an extended node clearance including coeliac, common hepatic and related nodes (R_2) as practised in Japanese centres then a palliative and a curative resection differ substantially. We have not studied the value of intra-operative microscopy in this setting and so concede that lymph node assessment – probably of the N_3 tier – might avoid an extended node clearance in incurable patients although we know of no study which has shown this.

References

1. Harmer MH, ed. UICC TNM classification of malignant tumours. 3rd ed. Geneva: UICC, 1978: 63–7.
2. Armstrong CP, Dent DM. Factors influencing prognosis in gastric carcinoma. *Surg Gynecol Obstet* 1986; **162**: 343–8.
3. Miwa K. Cancer of the stomach in Japan. *Gann* 1979; **22**: 61–75.
4. Fielding JWL, Roginski C, Ellis DJ *et al.* Clinicopathological staging of gastric cancer. *Br J Surg* 1984; **71**: 677–80.
5. Coit DG, Brennan MF. Gastric cancer. In: Moody FG, Carey LC, Jones RS *et al.*, eds. *Surgical Treatment of Digestive Disease.* Chicago: Year Book Medical Publishers, 1986, 239–56.
6. Japanese Research Society for Gastric Cancer. The general rules for the gastric cancer study in surgery and pathology. Part 1. Clinical classification. *Jap J Surg* 1981; **11**: 127–39.
7. Kennedy BJ. Staging of gastric cancer. *Semin Oncol* 1985; **12**: 19–20.
8. Nakajima T, Kajitani T. Surgical treatment of gastric cancer with special reference to lymph node dissection. *Excerpta Medica* 1981: 207–25.
9. Morris DL, Moore J, Thompson H, Keighley MRB. Accuracy of per-operative lymph node cytology in gastric carcinoma. *Clin Oncol* 1982; **8**: 219–21.
10. British Stomach Cancer Group. Resection line disease in stomach cancer. *Br Med J* 1984; **289**: 601–3.

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Present status of pharyngogastric anastomosis following pharyngolaryngo-oesophagectomy

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Pharyngolaryngo-oesophagectomy with pharyngogastric anastomosis was described more than 25 years ago. Since then it has been employed for the treatment of cancers of the hypopharynx, cervical oesophagus and larynx. Results of recent reports showed a wide variability. Our previous report of 157 such operations gave a significant morbidity and overall hospital mortality rate of 31 per cent. In the 6-year period between 1980 and 1985, 91 patients underwent this operation. The morbidity and mortality rates gradually decreased to 30 and 5 per cent respectively. Changes in the indications for the operation resulted in a reduction in the number of procedures performed in recent years. Resection of the oesophagus for cancers of the pharyngolaryngeal region is indicated only when there is actual oesophageal involvement, and would be the prime indication of pharyngogastric anastomosis.

Keywords: Pharynx, oesophagus, larynx, neoplasm

In the 1940s and 1950s the mainstay of treatment for carcinoma of the hypopharynx was radiotherapy. A major reason for the choice of this treatment was the inadequacy of operative procedures, which often involved multistaged reconstruction methods using local or regional skin flaps. While efforts were spent in trying to find an acceptable design for reconstruction of the hypopharynx and cervical oesophagus with local tissues, development in oesophagoplasty demonstrated that the stomach could be brought to the apex of the pleural cavity. In 1958 Ong and Lee brought the stomach to the neck to replace the hypopharynx and the entire oesophagus and reported their first three cases[1]. In retrospect it was a natural progression of oesophagoplasty and an expected milestone in the development of oesophageal surgery. That marked the beginning of two decades of experience in the application of the procedure for treatment of cancer of this region of the alimentary tract.

When the procedure was first described it involved three phases: laparotomy for preparation of the stomach, thoracotomy for oesophageal resection and cervical exploration for pharyngogastric anastomosis. Le Quesne and Ranger[2] described a modification of the procedure in 1966, in which thoracotomy was omitted. The thoracic oesophagus was removed by blunt dissection via the hiatus. The advantages of this change have since been recognized. Delivery of the stomach up the posterior mediastinum vacated by the oesophagus is now the standard procedure, and has often been described as the 'gastric pull-up' operation. We prefer to refer to the reconstructive effort as 'pharyngogastric anastomosis' and the resection process as 'pharyngolaryngo-oesophagectomy'. The original indications for this operation were cancers of the hypopharynx and cervical oesophagus. The procedure was subsequently employed for carcinomas of the larynx which had invaded the hypopharynx[3].

Since the first descriptions in the 1960s, numerous reports of the procedure have been published (*Table 1*)[1–24]. Our group from the University of Hong Kong, Queen Mary Hospital, presented a series of 157 patients in 1981[3]. Since then many more patients have been subjected to this procedure. The technique has undergone some refinement, the indications have been modified, and the results have changed. This article presents our recent results and our current attitude towards the procedure of pharyngogastric anastomosis after pharyngolaryngo-oesophagectomy.

Table 1 *Published results of pharyngogastric anastomosis*

Authors	Year	No. of patients	Hospital mortality (*n*)	Hospital mortality (%)
Ong and Lee[1]	1960	3	0	0
LeQuesne and Langer[2]	1966	10	3	30
Balasegaram[4]	1968	6	1	17
Leonard and Maran[5]	1970	10	2	20
Stell[6]	1970	19	5	26*
Stell[7]	1973	24	11	46
Millar[8]	1973	4	1	25
Akiyama *et al.*[9]	1975	21	0	0
Silver[10]	1976	6	2	33
Shepperd[11]	1977	19†	4	21
Cordiano *et al.*[12]	1979	7	0	0
Bains and Spiro[13]	1979	16	0	0
Effron *et al.*[14]	1979	4	0	0
Harrison *et al.*[15]	1981	58	6	10‡
Lam *et al.*[3]	1981	157	48	31
Fredrickson *et al.*[16]	1981	9	0	0
Mannell and Davidge-Pitt[17]	1981	6	0	0
Silver[18]	1981	9	3	33
Peracchia *et al.*[19]	1982	32	5	16
Spiro *et al.*[20]	1983	63	6	10
Stell *et al.*[21]	1983	35§	18	51
Pradhan and Rajpal[22]	1984	25	5	20
Surkin *et al.*[23]	1984	12	1	8
Jones *et al.*[24]	1986	16	8	50
Total¶		495	104	21

*Mortality defined as death within 3 weeks
†Excluding 4 in whom procedure not completed
‡Mortality defined as death at or soon after operation
§Included reconstruction using colon
¶Stell 1970[6], Silver 1976[10], Bains and Spiro 1979[13], Stell *et al.* 1983[21] excluded because cases included in later reports or because exact number of cases uncertain

Material

The records of the Department of Surgery in the Queen Mary Hospital, University of Hong Kong, from 1980 to 1985 were reviewed. Patients who had undergone pharyngolaryngo-oesophagectomy and pharyngogastric anastomosis as the initial surgical procedure were

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identified. Included were patients who were referred when control of tumour by radiotherapy had failed. Those in whom the operation had been performed as a salvage procedure for postoperative complications or for local recurrence after total laryngectomy were excluded.

Between 1980 and 1985, 73, 21, and 316 patients were admitted with the diagnosis of carcinoma of the hypopharynx, cervical oesophagus, and the larynx respectively (*Table 2*). Among them 56, 15 and 230 were treated surgically, either alone or as part of a combined treatment schedule. The procedure performed was pharyngolaryngo-oesophagectomy in 41 (56 per cent), 11 (52 per cent), and 39 (12 per cent) respectively, making a total of 91 patients. Carcinoma of the larynx is usually localized and required only total or other forms of laryngectomy, hence the few patients treated. In one of the patients with carcinoma of the hypopharynx there was a second primary squamous cell carcinoma in the middle thoracic oesophagus.

To illustrate the changing indications and practice over the period of study, the patients are separated into groups each extending over 2 years (*Table 3*). The number of patients treated surgically are shown together with the number of patients who have undergone pharyngolaryngo-oesophagectomy–pharyngogastric anastomosis. It is seen that the proportion of patients undergoing pharyngolaryngo-oesophagectomy–pharyngogastric anastomosis for hypopharyngeal cancer decreased progressively over the three periods. This is more marked with respect to laryngeal carcinoma patients. For carcinoma of the cervical oesophagus, no such trend is apparent, although the number of patients is small.

The other operative procedures performed for cancer of the hypopharynx were partial pharyngectomy or total pharyngectomy without thoracic oesophagectomy, and myocutaneous flap reconstruction. For cervical oesophageal cancer the other infrequently performed operation for low-lying tumours was total oesophagectomy without pharyngolaryngectomy. For cancer of the larynx, partial pharyngectomy with total laryngectomy was often carried out together with myocutaneous flap repair.

Among the 91 patients who had undergone the operation of pharyngolaryngo-oesophagectomy–pharyngogastric anastomosis, there were 82 men and 9 women (ratio of 9:1). Their mean age was 60 years. Previous radiotherapy had been given in 11 (27 per cent) of the 41 patients with hypopharyngeal cancer, 2 (18 per cent) of the 11 patients with cervical oesophageal cancer, and 21 (54 per cent) of the 39 patients with laryngeal cancer. Cervical lymph node enlargement was found in 17 (2 bilateral) 1 and 17 (3 bilateral) patients respectively. Radical neck dissection was carried out as part of the operation in 25 (13 bilateral), 3 (2 bilateral) and 18 (4 bilateral) respectively.

Table 2 *Surgical treatment of patients*

	Hypopharynx	Cervical oesophagus	Larynx
Total no. of patients	73	21	316
No. operated upon	56	15	230
PLO–PGA*	41 (56%)	11 (52%)	39 (12%)

*PLO–PGA, Pharyngolaryngo-oesophagectomy and pharyngogastric anastomosis

Table 3 *Changing frequency of pharyngolaryngo-oesophagectomy and pharyngogastric anastomosis (PLO–PGA) as operative treatment*

	Hypopharynx*	Cervical oesophagus*	Larynx*	Total
1980–81	11/12 (92%)	7/9 (78%)	20/61 (33%)	38
1982–83	17/18 (94%)	1/1 (100%)	13/78 (17%)	31
1984–85	13/26 (50%)	3/5 (60%)	6/91 (7%)	22
Total	41/56	11/15	39/230	91

*PLO–PGA/Total number treated surgically

Results

The mortality and morbidity of the patients after the operation are shown in *Table 4*. Mortality is defined as death in hospital after operation, irrespective of the length of the postoperative period. The results of our previous report, concerning patients up to 1979[3], are also shown for comparison. It is apparent that there is a gradual drop in hospital mortality, until a level of around 5 per cent is reached.

Of the ten hospital deaths in the present series, the majority died from chest infection (six) and persistent sepsis in the neck (two). One patient died from recurrent tumour in the neck two months after operation. The remaining one died from acute haemorrhage from the tracheostomy, probably from an eroded innominate artery as a result of receding trachea after manubrium resection. In addition to this last patient, three had bleeding from the neck before dying from pulmonary and cervical sepsis although they did not die directly from it. The sites of haemorrhage were the common carotid, the stump of the external carotid and the edges of the pharyngogastric anastomosis. Reduction of postoperative complications such as these was associated with a drop in hospital mortality.

The overall morbidity has also come down to around 30 per cent. The incidence of anastomotic leakage was below 10 per cent and the problems of wound sepsis and postoperative haemorrhage were reduced to about 5 per cent. Approximately one-fifth of the patients have some degree of chest infection.

Discussion

As seen in *Table 1*, which summarizes the published reports on the use of the whole stomach for reconstruction after pharyngolaryngeal resection, the major experiences appeared in the 1980s. The total number of operations included in these reports is about 500. The overall hospital mortality, 104 cases, was 21 per cent. The mortality of the individual series varied very widely, from 0 to 51 per cent. The reasons for the range in mortality include differences in definition, patient selection, operative technique and experience. The mortality rate in some series is so high as to cast doubt on the advisability of the operation. The justification for continuing to carry out the procedure is the need to palliate the symptom of dysphagia in these unfortunate patients who would have an overall survival of about 12 months.

In spite of our initial high operative risk, the procedure was continued. This was the only operation suitable for tumours located at the hypopharynx, cervical oesophagus, and for laryngeal cancers extending to the hypopharynx, until other reliable single-stage methods of pharyngeal reconstruction became available. As we persevered, refinement of operative technique and attention to detail limited many serious postoperative complications. The hospital mortality of our last 91 patients was thus markedly reduced. During this period,

Table 4 *Mortality and morbidity after pharyngolaryngo-oesophagectomy and pharyngogastric anastomosis*

	No.	Mortality (%)	Anastomotic leak (%)	Wound sepsis (%)	Neck haemorrhage (%)	Chest infection (%)	Overall morbidity (%)
Up to 1979*	157	31	23	27	20	27	—
1980–1	38	18	18	34	16	29	53
1982–3	31	6·5	6·5	6·5	3·2	13	29
1984–5	22	4·5	9	4·5	4·5	18	32

*From Lam *et al.* 1981[3]

some selection of patients has taken place, not in terms of exclusion of higher risk patients, but in terms of prescribing a different procedure when the indication for total oesophagectomy was not present.

With rapid development of new and revised methods of reconstruction of the hypopharynx and cervical oesophagus, there is choice of procedure. In fact the reconstructive technique is dependent on the type of defect, and for each type of defect the choice of repair is limited unless the type of defect is modified to suit the reconstructive surgeon's preference. Such action is not warranted, because any reduction of size of the defect may compromise tumour clearance, while enlargement of the defect, entailing loss of normal tissue, will increase the complexity of the operation and affect postoperative function. A resection margin of 30 mm would generally be adequate, and no further sacrifice of normal tissue should be necessary.

We have classified the growth of tumours arising from the cervical oesophagus, hypopharynx and larynx into the following three patterns and have defined the limits of resection for each pattern. If the tumour arises from the cervical oesophagus, or involves the cervical oesophagus, spreading from either the hypopharynx or the larynx, a total oesophagectomy will be required, together with pharyngolaryngectomy. The defect will extend between the base of the tongue and the cardia. For lower hypopharyngeal tumours and laryngeal tumours spreading to the lower hypopharynx, but sparing the cervical oesophagus, total (circumferential) pharyngectomy together with resection of at least 3 cm of cervical oesophagus is necessary. The defect will lie between the base of the tongue and the distal 1 or 2 cm of the cervical oesophagus. If the tumour affects only the upper part of the hypopharynx, either originating from it or spreading to it from the larynx, partial pharyngectomy with total laryngectomy should be performed. The hypopharyngeal defect will lie between the base of the tongue and the upper end of the cervical oesophagus, but affecting the anterior aspect only. Because of these redefined patterns of radical resection, the number of patients undergoing total pharyngolaryngo-oesophagectomy has reduced and thus the number of pharyngogastric anastomoses has decreased in recent years.

For the total pharyngolaryngo-oesophagectomy defect, we regularly used the whole stomach for reconstruction, brought up through the posterior mediastinum. We preferred the stomach to bowel loops because of its reliability, ease of preparation and simplicity in reconstruction. The pharyngogastric anastomosis is the only anastomosis required. The colon would be the next choice, though it requires good pre-operative preparation and three anastomoses are necessary instead of one. A longer length of colon can be prepared than the third choice, the jejunum. Operative technique in the preparation of the latter is more demanding.

For circumferential defects, with an intact oesophagus, we used the tubed pectoralis myocutaneous flap for reconstruction. Our technique, modified to avoid stenosis at the mucocutaneous suture-lines, has been described[25]. Our initial experience with six patients showed promising results[26] in that stricture had not occurred. Other tubed flaps such as the latissimus dorsi myocutaneous flap[27] and the radial forearm flap[28], requiring microvascular anastomosis, can be used in the same manner. They have no advantage over the pedicled pectoralis flap. Free jejunum loop has been established as reliable[29], and has the advantage of being a mucosa lined conduit without a longitudinal suture line. Neck skin flaps and deltopectoral flaps should no longer be used as they are multistaged and not reliable.

For partial defects of the pharyngeal wall, our preference is for a patched-on pedicled pectoralis myocutaneous flap[30]. Any other pedicled island flap, without the need for a temporary salivary fistula, is acceptable, but free skin flaps and free intestinal patch-on grafts are unnecessarily complicated.

While pharyngogastric anastomosis has definite advantages, there are limitations. The first is the limitation of its reach. The stomach can comfortably join to the oropharynx at the level of the base of the tongue or the tonsil, but would give rise to tension on the suture line if the anastomosis lies in the nasopharynx. If on clinical examination the tumour can be seen with the help of a tongue depressor, it is probably too high for the stomach to reach after taking adequate margins of clearance. Fortunately, high tumours do not extend downwards, unless they are huge. Thus cervical reconstruction with myocutaneous flaps or free jejunal grafts are applicable. Secondly, it is obvious that the operation is not possible if the stomach has been resected.

With respect to long term problems[20,31], severe disability was minimal. Regurgitation, however, is a significant symptom present in about a quarter of patients. This, as well as the occasional gastric complications of gastritis and ulceration, will be avoided if the oesophagus is not resected and replaced with the stomach.

In conclusion, we have demonstrated that while the hospital mortality of the operation of pharyngolaryngo-oesophagectomy and pharyngogastric anastomosis can be reduced to an acceptable level, the indications for operation are more defined, and its application should not be abused.

References

1. Ong GB, Lee TC. Pharyngogastric anastomosis after oesophago-pharyngectomy for carcinoma of the hypopharynx and cervical oesophagus. *Br J Surg* 1960; **48**: 193–200.
2. LeQuesne LP, Ranger D. Pharyngolaryngectomy, with immediate pharyngogastric anastomosis. *Br J Surg* 1966; **53**: 105–9.
3. Lam KH, Wong J, Lim STK, Ong GB. Pharyngogastric anastomosis following pharyngolaryngoesophagectomy analysis of 157 cases. *World J Surg* 1981; **5**: 509–16.
4. Balasegaram M. Pharyngo-gastric reconstruction for carcinoma of the hypopharynx. *Aust NZ J Surg* 1968; **37**: 242–8.
5. Leonard JR, Maran AGD. Reconstruction of the cervical esophagus via gastric anastomosis. *Laryngoscope* 1970; **80**: 849–62.
6. Stell PM. Esophageal replacement by transposed stomach following pharyngolaryngo-esophagectomy for carcinoma of the cervical esophagus. *Arch Otolaryngol* 1970; **91**: 166–70.
7. Stell PM. Cancer of the hypopharynx. *J R Coll Surg Edinb* 1973; **18**: 20–30.
8. Millar H. The surgical treatment of cervical oesophageal and laryngopharyngeal dysphagia. *Aust NZ J Surg* 1973; **42**: 368–73.
9. Akiyama H, Hiyama M, Miyazono H. Total esophageal reconstruction after extraction of the esophagus. *Ann Surg* 1975; **182**: 547–52.
10. Silver CE. Reconstruction after pharyngolaryngectomy-esophagectomy. *Am J Surg* 1976; **132**: 428–34.
11. Shepperd HWH. Surgery for the post-cricoid carcinoma. Report on 23 cases in which replacement by stomach was attempted. *J Otolaryngol* 1977; **6**: 271–6.
12. Cordiano C, Fracastoro G, Mosciaro O, Mozzo W. Esophagectomy and esophageal replacement by gastric pull-through procedure. *Int Surg* 1979; **64**: 17–25.
13. Bains MS, Spiro RH. Pharyngolaryngectomy, total extrathoracic esophagectomy and gastric transposition. *Surg Gynecol Obstet* 1979; **149**: 693–6.
14. Effron MZ, Myers EN, Rueger RG. Pharyngogastric reconstruction after esophago-pharyngolaryngectomy for carcinoma of the hypopharynx and cervical esophagus. *Pennsylvania Acad Ophthalmol Otolaryngol* 1979; **32**: 166–70.
15. Harrison DFN, Thompson AE, Buchanan G. Radical resection for cancer of the hypopharynx and cervical oesophagus with repair by stomach transposition. *Br J Surg* 1981; **68**: 781–3.
16. Fredrickson JM, Wagenfeld DJH, Pearson G. Gastric pull-up vs deltopectoral flap for reconstruction of the cervical esophagus. *Arch Otolaryngol* 1981; **107**: 613–16.
17. Mannell A, Davidge-Pitts K. Pharyngeal reconstruction after pharyngolaryngoesophagectomy in African patients. *Aust NZ J Surg* 1981; **51**: 603–9.
18. Silver CE. Surgical treatment of hypopharyngeal and cervical esophageal cancer. *World J Surg* 1981; **5**: 499–507.
19. Peracchia A, Ancona E, Buin F. The surgical treatment of cancer of the cervical esophagus: complications and preliminary results. *Int Surg* 1982; **67**: 135–7.
20. Spiro RH, Shah JP, Strong EW, Gerold FP, Bains MS. Gastric transposition in head and neck surgery. *Am J Surg* 1983; **146**: 483–7.

21. Stell PM, Missotten F, Singh SD, Ramadan MF, Morton RP. Mortality after surgery for hypopharyngeal cancer. *Br J Surg* 1983; **70**: 713–18.
22. Pradhan SA, Rajpal RM. Gastric pull-up for cancers of the hypopharynx and cervical esophagus: our experience. *J Surg Oncol* 1984; **26**: 149–52.
23. Surkin MI, Lawson W, Biller HF. Analysis of the methods of pharyngoesophageal reconstruction. *Head Neck Surg* 1984; **6**: 953–70.
24. Jones PH, Farrington WT, Weighill JS. Surgical salvage in postcricoid cancer. *J Laryngol Otol* 1986; **100**: 85–95.
25. Lam KH, Wei WI, Lau WF. Avoiding stenosis in the tubed greater pectoral flap in pharyngeal repair. *Arch Otolaryngol* 1986, in press.
26. Lam KH, Wei WI. Some special elective surgical techniques – cervical and post-cricoid lesions. In: Delarue NC, Eschapasse H, eds. *International Trends in General Thoracic Surgery*. Volume V. Philadelphia: W.B. Saunders Co. 1986 in press.
27. Watson JS, Robertson GA, Lendrum J, Stranc MF, Pohl MJ. Pharyngeal reconstruction using the latissimus dorsi myocutaneous flap. *Br J Plast Surg* 1982; **35**: 401–7.
28. Harii K, Ebihara S, Ono I, Saito H, Terui S, Takato T. Pharyngoesophageal reconstruction using a fabricated forearm free flap. *Plast Reconst Surg* 1985; **75**: 463–76.
29. Robinson DW, Macleod A. Microvascular free jejunum transfer. *Br J Plast Surg* 1982; **35**: 258–67.
30. Withers EH, Franklin JD, Madden JJ, Lynch JB. Immediate reconstruction of the pharynx and cervical esophagus with the pectoralis major myocutaneous flap following laryngopharyngectomy. *Plast Reconst Surg* 1981; **68**: 898–904.
31. Wei WI, Lam KH, Choi S, Wong J. Late problems after pharyngolaryngoesophagectomy and pharyngogastric anastomosis for cancer of the larynx and hypopharynx. *Am J Surg* 1984; **148**: 509–13.

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Arrow wounds to the heart and mediastinum

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Wooden tipped arrows are still used in tribal fighting in the Highlands of Papua New Guinea. Thirteen cases of arrow injury to the heart and mediastinum, presenting at Mt. Hagen Hospital in a 2-year period, are described. Ten cases presented early (within 3 days) while the remaining 3 cases presented late and suffered from mediastinal abscesses. Removal of the arrow, after full visualization with repair where possible, was performed in all cases with two deaths and little morbidity. Most of the 13 patients arrived in a stable condition, withstood surgery well and made a rapid recovery (average stay in hospital 20 days). Unstable presentations included 2 cases of mild shock, one with early cardiac tamponade and one case of acute aortic incompetence. Survival figures justify attempted salvage of these patients, even with the limited facilities available.

Keywords: Tropical medicine, thoracic surgery, cardiac surgery, mediastinal abscess

Tribal fighting still goes on around Mt. Hagen and, although Western influence has penetrated most other areas of their culture, the Highlanders have retained all their traditional skills and weapons when it comes to solving intertribal conflicts. These conflicts may go back many generations and it is a matter of pride for the present generation of warriors to keep using the same type of weapons and the same strategy as their forefathers. This consists of direct confrontation with bows and arrows (shafts of bamboo, each tipped with a narrow piece of hardwood about 18 inches long sharpened to a fine point, without any flight stabilizers). Ambush and hand-to-hand combat were not often employed in a formal tribal flight, so we only occasionally saw axe wounds.

Common sites of arrow injuries are the orbit and the knee joint (cavities above and and below the shield, soft tissue sites being treated on the field or at local health centres), the left axilla (under the bow arm in extension, the victim aiming through a gap in his own army's front line shield defence) and the root of the neck, travelling down into the chest (sustained while crawling up a hill towards the enemy). Intra-abdominal injuries were rare, but posterior shots into the retreating body (spinal cord and kidney) were encountered.

This paper gives the details of 13 patients who presented over a 2-year period to Mt. Hagen Hospital with arrow wounds involving the mediastinium. Twenty-one other patients presented with arrow wounds which required thoracotomy but they are not considered further in that major mediastinal structures were not involved.

Table 1 *Patient condition on arrival at hospital*

Diagnosis	Number of cases
Acute arrow injury	
Stable	5
Shock	2
Cardiac tamponade	1
Acute aortic incompetence	1
Haemoptysis	1
Mediastinal abscess	
Stable	2
Septic	1

Table 2 *Results of pre-operative chest X-rays in patients with arrow injury*

Report	Number of cases
Normal	2*
Widened mediastinum	2†
Haemothorax	1
Haemopericardium plus haemothorax	1‡

*One patient had a human bone arrow shown in a mediastinal abscess
†One patient had an associated haemothorax and both were in shock
‡This patient did not present with cardiac tamponade

Patients and methods

The period of review extended from June 1983 to July 1985. The 13 patients arrived at the hospital after a variable delay following their injury. This reflects the isolated areas where the tribal fight was taking place (to avoid the police helicopter with tear gas!), poor means of transport and reluctance to travel through enemy territory. Ten patients arrived within three days of their injury and were classed as acute arrow injuries. The remaining 3 patients, all with mediastinal abscesses, arrived 12 days, 2 weeks and 6 months later. The condition of patients on arrival is given in *Table 1*. Immediate surgery was undertaken on the 5 patients with acute arrow injuries who presented with complications, otherwise surgery was delayed until later in the day if convenient, or the next day if suitable.

The history from the patient and his 'wantoks' (members of the same tribe) was always believed, so if they said an arrow was still inside the patient then surgery was undertaken. Usually a reliable history could be obtained as to how far the arrow went in, although occasionally it was uncertain if all the arrow had been removed. In 7 of these cases, the arrow was protruding from the skin, having been broken off at skin level; in 4 cases we were told that the arrow was still inside the patient (and we found it on every occasion) and the remaining 2 patients, where the arrow had been removed on the battle field, required surgery to assess the injury adequately (one case had haemoptysis from a hilar injury and the other had a small puncture wound just to the left of the sternum in the fourth intercostal space (ICS) and was found to have a perforated right ventricle).

The only pre-operative investigation was an erect chest P–A X-ray, undertaken on 6 patients (see *Table 2*). As conservative management was not often employed, the problems of transporting a patient to the X-ray department, the scarcity of X-ray film and the fact that wooden arrows were radiolucent, meant that the procedure was often not justified.

The arrow, if protruding, was not disturbed during preparation of the patient, or during the incision and initial exploration. Arrows entering the root of the neck (3 patients) were explored via a collar incision, median sternotomy to the fifth ICS, then extension laterally (to the side of the pathology) with the raising of a large flap consisting of the upper three or four ribs. Arrows lodged in the sternum (4 patients), were approached through double anterior thoracotomies joined in the centre

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with division of the sternum at the level (usually the fourth or fifth ICS). The arrow could then be divided under the sternum with the sternal cutter before wide sternal retraction was performed. The remaining 6 cases, where the arrow entered via an ICS, were explored through an anterior thoracotomy, often with the resection of several costal cartilages to raise a flap of ribs. In 2 of these cases, damage to the mediastinum was not diagnosed pre-operatively (one pericardial laceration and one penetration of the left ventricle).

Most patients received pre-operative and intra-operative digoxin and a xylocaine infusion, remaining on digoxin during their hospital stay and on the xylocaine infusion for one or two days postoperatively. One patient with an irregular heart beat postoperatively (frequent extrasystoles) remained on a xylocaine infusion for several days. An irregular heart beat was not detected pre-operatively in any patient.

Following exposure of the arrow, the extent of the injury was assessed. A list of the structures involved is given in *Table 3*. Dissection always exposed the tip of the arrow before withdrawal was attempted. If the arrow had perforated the heart, the posterior surface of the heart was palpated. In one case, the arrow extended from the sternum, through both ventricles, and the posterior descending coronary artery into the soft tissue around the spine – completely transfixing the heart. Following removal of the arrows from the heart, any perforations were allowed to spurt for a few beats to clear any clots. The wounds were then oversewn with interrupted 2/0 prolene sutures placed while bleeding was controlled with the left index finger. A posterior perforation was approached by elevating the heart for short periods. Any perforation involving a major coronary artery (2 cases) was controlled by suture ligation. The pericardium was left wide open; on one occasion this was the sole mediastinal part of the operation. Perforations of the major vessels were treated by proximal and distal suture ligation (right brachiocephalic vein), vein graft (left common carotid artery repaired by left brachiocephalic vein) or suture repair (ascending aorta).

Abscesses were gently debrided and drained. One abscess involved the right ventricle at the tip of the arrow and debridement resulted in perforation of the right ventricle. This was oversewn using 2/0 prolene and was not a problem postoperatively. One patient with a mediastinal abscess presented six months following his injury and an arrow of human bone was found penetrating the right chest obliquely (fourth ICS) before entering the anterior mediastinum. This was the only case we encountered of an arrow of bone (prepared by sharpening the ulna or fibula of an enemy from a previous tribal fight). The arrow was palpable beneath the skin and was removed. The cavity was then drained with a satisfactory outcome.

Table 3 *Structures involved by arrow injury*

Organ	Number of cases
Heart	
Right ventricle alone	3*
Left ventricle alone	1
Right and left ventricles and posterior descending coronary artery	1
Right auricle, right coronary artery and aortic valve	1
Major vessel	
Right brachiocephalic vein	1
Left common carotid artery	1
Ascending aorta	1
Mediastinal tissue (abscess)	3*
Hilum of left lung	1
Pericardium	1
	14*

*In one of mediastinal abscess, the arrow also perforated the right ventricle

One patient had a small perforation at the hilum of the left lung, the arrow having slipped down between lung and mediastinum from the left infraclavicular region. This arrow had been removed on the battlefield and the patient was brought to us on the same day complaining of haemoptysis. Chest X-ray revealed a left haemothorax and an opaque left upper lobe. At surgery the next day, there was a moderately sized haemothorax and a considerable haematoma in the left upper lobe extending from the hilum. No active bleeding was found and mediastinal emphysema was not evident. Blood stained sputum was aspirated from the left bronchus.

Exploration of the hilum was undertaken and, although the pulmonary artery was found to be normal, the other structures were not adequately exposed. Increased ventilation pressure through a single lumen endotracheal tube did not reveal any bronchial leak. Postoperatively he developed a high fever with sputum retention and collapsed left upper lobe. During bronchoscopy two days later he died from cardiorespiratory arrest. The exact cause was not obvious and post mortem was refused.

In 3 patients, associated perforation of the lung was found. As there was no major bronchiolar leak or bleeding from the lung tissue in any of these cases, the lung tissue wounds were left open for drainage.

Results

There were 2 deaths in these 13 cases. The one case following hilar injury has already been discussed. The other involved an arrow which passed through the right auricle, origin of the right coronary artery and then through the aortic valve. When the patient presented a thrill was palpable over the sternum, a loud murmur was present and the blood pressure was 100/40 mmHg. Death occurred 1 hour following surgery (oversewing the perforation and ligation of the coronary artery). Aortic incompetence persisted following removal of the arrow and this, combined with a probable myocardial infarction, was the cause of death. In another patient the posterior descending coronary artery was oversewn about half-way along its course without any clinical problem. In no other cases did valvular incompetence or septal perforation cause any problems, although a pansystolic murmur persisted in one patient up to the time of discharge.

A list of postoperative complications is given in *Table 4*. The wound infection followed a large anterolateral thoracotomy in a patient with an associated injury to the left lower lobe. The patient who developed transient cardiac failure was the one in whom the abscess eroded into the right ventricular wall. The pleural effusion, requiring two aspirations to clear up, followed suture ligation of the right brachiocephalic vein and, being on the same side as the extensive dissection, may well have been a chylothorax. The patient whose left branchiocephalic vein was used as a graft developed a transient oedema of his left arm although extravasation from his intravenous infusion rather

Table 4 *Results of treatment of arrow injury*

Diagnosis	Number of cases	Postoperative complications	Deaths	Length of stay in survivors (days)
Injuries to the heart (acute presentations)	5	Transient arrhythmia (1)* Persistent pansystolic murmur (1)* Wound infection (1)	1	15,18,19,20
Mediastinal abscess	3	Bronchospasm/pneumonia (1) Cardiac failure (1)	Nil	17,20,34
Major vessel injury	3	Pleural effusion (1) Oedema of arm (1)	Nil	15,15,26
Pericardial laceration	1	Nil	Nil	14
Hilum left lung perforation	1	—	1	

*These two complications occured in the same case, a perforated right ventricle than venous obstruction was probably responsible. His arm was normal on discharge 15 days postoperatively.

The length of stay in hospital is also given in *Table 4*. Not one of the 11 cases returned for follow-up, highlighting the problems these people have in leaving their home territory. Surgery was always performed with the relatives of the patient watching through the window and one or two of his closest family actually in the operating theatre, just to check on what was happening to their 'wantok'. On one occasion we had two patients from opposing tribes in the same ward. Both had arrows in their hearts. Although the hospital was regarded as neutral territory, no-one slept much in the ward until they could be separated!

All injuries to the heart were either central or on the left side of the chest, except the long standing injury inflicted by the arrow of human bone. There were no tracheal or oesophageal perforations from arrows, although we treated one of each from a knife and a stake wound respectivley during the 2-year period. We did not encounter nerve palsies, either on presentation or postoperatively.

Discussion

Arrows protruding from the body were not removed by the tribesmen and were not removed by us until the extent of injury was fully visualized. Removal from the heart or major vessels usually resulted in a gush of blood, although there was one case of a punctured right ventricle where the arrow had come out before admission, without a disastrous result. There were three patients with barbed arrows in this series, and one arrow was made from human bone. The four cases were the only examples of these types of arrows we encountered in the hundreds we removed from all over the body. Apparently these prized arrows are only used for very close shots at the heart. We were amazed at the strength of the wooden arrow, which easily penetrated the sternum to a depth of 3 or 4 inches. Removal of the arrow from the sternum was a difficult procedure – we used chisels and drills to dislodge them, leaving a hole in the sternum about 1 inch in diameter. These wounds were usually approached through a separate incision and then closed primarily. We had no deep infections, which may reflect the sensitivity of the organisms to our antibiotics, resistance having not yet developed. The arrows themselves are very clean and are stored in the roof of the huts where the warriors live, and so are exposed to the smoke and heat of the fire always alight inside. This made the wood very hard and may have kept the bacterial count low.

There were no clinical cases of pulmonary or peripheral emboli during or after surgery. No prophylactic measures were employed and, during my time at Mt. Hagen, I never saw a case of deep vein thrombosis or pulmonary emboli. The two deaths in this series deserve some comment. In the patient with injury to the hilium of the left lung, more thorough dissection at the hilium may have revealed a bronchopulmonary fistula, and it is arguable that left upper lobectomy should have been performed to remove infarcted lung tissue. Given the facilities available it is difficult to know what could have been done to avoid the second death in the series where aortic incompetence was undoubtedly a major contributory factor.

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Dr Alan Kulunga contributed many of the facts and theories I have used in relation to tribal customs, the nature and types of injuries, and the pathogenesis of the infectious process in these types of wounds. I thank him for this and I also thank Dr Roy Kirkpatrick, Dr Weston Seta, Dr Ikau Kevau and Dr Kana Eorage for their help in the management of these patients.

References

1. Fingleton LJ. Bush thoracotomy in the Highlands of Papua New Guinea. *Br J Surg* 1987; 74: 129–32.

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Bush thoracotomy in the Highlands of Papua New Guinea

Bush thoracotomy is a procedure performed by traditional medicine men to let out blood and pus from the chest. It has a significant complication rate and 60 cases presenting to the major hospital in Papua New Guinea are analysed over a 2-year period. The complications were empyema (40), osteomyelitis of the rib (2), wound infection (2), pneumothorax (1), neuralgia (1) and chest pain (4). All cases were further complicated by underlying pulmonary infection and often by delay in presentation. Fifteen cases were seen in the first year (1983–84) and forty-five in the second (1984–85). A more aggressive surgical approach was adopted in the second year (21 thoracotomies with 17 decortications compared with 1 thoracoplasty in the first year). However, this course of events was accompanied by an increase in mortality from 0 to 5. Although there were a number of contributory factors, lesser surgical procedures, such as open pleural drainage, are recommended for the sicker patients.

Keywords: Tropical medicine, empyema, osteomyelitis, thoracic surgery, drainage, thoracoplasty, decortication

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While I was working at Mt. Hagen Hospital in the Highlands of Papua New Guinea, it was not uncommon to come across a thin, wasted young male warrior, sitting on the floor of the ward, coughing up pus between gasps of breath. He would have sweat pouring off him and a bark bandage surrounding his chest, with pus oozing out through the leaf-dressing underneath. He was suffering from the complications of a 'bush thoracotomy'[1,2].

Mt. Hagen Hospital has 210 beds with 70 allocated to surgery, although there are always more patients than beds. It provides the only specialized surgical service for over half a million people. After I arrived in June 1983, the unit consisted of a registrar, houseman and myself but this was later expanded by a second surgeon and another registrar. Anaesthetics were performed by very competent technicians. Back-up services consisted of radiology (plain X-rays and intravenous pyelograms), haematology (Hb, WCC and ESR), microbiology (Gram stain only) and blood bank (a very good supply of cross-matched blood). Biochemistry and more extensive haematology took several days via the main hospital in Port Moresby, if one could justify the expense. The surgical unit averaged 300 operations a month, mostly for infections and trauma, but we were not the only ones performing 'specialized surgery'.

Bush thoracotomy is a procedure performed in the villages of Western Enga Province. Stab incisions using sharpened bamboo are made into the chest by the local bush doctor to let out blood and pus. Usually two incisions are made on the offending side – one anterior in the third intercostal space in the mid-clavicular line and the other in the seventh intercostal space in the anterior axillary line. Free drainage is allowed into a dressing of banana leaves. Indications vary enormously, although the commonest is an arrow wound to that side of the chest. Any injury to the upper trunk or shoulder–neck region that results in pain may lead the victim to suspect blood or pus in his chest (even some years later) and he will submit to bush thoracotomy. It is impossible to estimate the number of these procedures being done – we sometimes saw the scars on patients coming from that area with other illnesses. What percentage develop complications requiring hospitalization is unknown as other hospitals and health centres care for some of these patients. However, Mt. Hagen Hospital is the only nearby hospital providing a specialized surgical service and as we adopted a sympathetic attitude towards them it is probable that we saw the majority of the sicker patients.

This paper shows how our treatment of the complications of bush thoracotomy changed over the 2-year period from June 1983 to June 1985, taking into consideration the limitations of our experience and the hospital facilities.

Methods

There were 60 patients admitted to Mt. Hagen Hospital in the 2 years up to July 1985 with one or more of the complications of bush thoracotomy. A list of the complications is given in *Table 1*; empyemas presented the major problem. We found it difficult to classify patients on admission into those with acute or chronic empyemas. Histories from these patients were unreliable owing to language problems and secrecy about a process which had a certain mystical flavour and which led to some ostracism by the rest of the society. Differentiation depended heavily on X-rays, gross pathology and response to treatment.

All patients with empyemas presented with chest pain, shortness of breath, cough and weight loss. The sickest ones were very hot and toxic, wasted, coughing up a lot of pus and very short of breath. The more chronic cases were associated with contraction deformities of the chest. The bush thoracotomy wound may be open (sucking and blowing air and pus), closed but discharging pus, or completely sealed. The nature of the wound does not always reflect the severity of the illness. However, the wasted toxic patient often had a large necrotic hole in his chest wall.

Chest X-rays (PA and lateral) were taken on admission and the haemoglobin concentration was determined. A typical chest X-ray showed elevation of the diaphragm, approximation of the ribs and displacement of the mediastinum, pleural thickening, collapsed lung and multiloculated fluid levels. However, the appearances ranged from a totally collapsed lung with no fluid level (open wound) to a massive single fluid level.

Chest pain was a constant feature but occasionally no cause could be found and it may have represented the indication for bush thoracotomy

Table 1 *Complications of bush thoracotomy*

Diagnosis	Number of cases admitted 1983–84	Number of cases admitted 1984–85
Empyema		
Acute	1	1
Chronic	9(3)	29(3)
Absconded	4	2
Refused treatment	1	1
Chest pain	—	4(1)
Osteomyelitis of rib	(2)	2[6](1)
Wound infection	—	2
Neuralgia	—	1
Pneumothorax	—	1
Lost notes	—	2
Total	15	45

(...) Represents possible diagnosis of those absconding, lost notes or refused treatment and sent home
[...] Represents incidental finding in empyema cases

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in the first place. Interpretation of chest X-rays in this group was often difficult, as appearances ranged from gross pleural thickening with tethering of the lung and diaphragm, to a normal picture. Lack of toxicity and response to analgesia helped to establish this diagnosis. One case of neuralgia was found, the diagnosis being confirmed by local anaesthetic block. Wound infection of the bush thoracotomy site was often present but was classified separately where it was the sole complaint, as was osteomyelitis of the ribs adjacent to the incision. One patient presented with a small pneumothorax and no other findings.

Results

In the 12-month period 1 July 1983 to 1 July 1984, 15 patients were admitted to the wards with one or more of the complications of bush thoracotomy. Our approach to the patients with empyema was basically conservative. Patients with haemoglobin levels below 10 mg/dl were given a blood transfusion and anti-malarial drugs. Dietary advice and chest physiotherapy were given to everyone, along with antibiotics. Depending on availability, chloramphenicol was usually prescribed for three or four weeks (combined with gentamicin for the first ten days if the patient was very toxic) then tetracycline or cloxacillin was given for three weeks and the patient was discharged home on Bactrim.

Generally two intercostal tubes (ICT) were inserted, although occasionally one was sufficient. Their sites depended on the X-ray findings of pus and adhesions, but usually we inserted an anterior apical Malecot catheter and a lateral, basal, very large red rubber tube drain (we had a plentiful supply of old No. 10 and No. 11 Magill endotracheal tubes). This basal tube insertion involved a 2-inch resection of rib which was usually one rib above and slightly behind the bush thoracotomy site, as the diaphragm often came up to seal off that level. Owing to shortages, these catheters were attached to one underwater drainage bottle. The tubes often needed irrigating and repositioning, eventually being shortened. Sometimes suction was used if a cavity persisted, but it never seemed to make any difference. When there was no swing in the water level of the bottle, no drainage and no evidence of a collection of pus on chest X-ray, the tubes were gradually withdrawn. Often pus would continue to drain without swing or X-ray evidence, in which case the tube was replaced by a small red rubber catheter and just allowed to drain into a dressing. Sinograms were performed on three patients at this stage but were not available after that and did not aid us in our management. Any small, new fluid levels appearing on chest X-ray were treated by aspirations and instillations of antibiotics. There were no complications or deaths with this approach. The one patient with an acute empyema was in hospital 9 days, while the nine patients with chronic empyema stayed an average of 63 days (range 35–98 days). The only woman (possible chronic empyema) and only child (possible osteomyelitis of the rib) in this group absconded.

One patient needed readmission for a persistent apical cavity which was treated by a posterolateral apical (three rib resection) thoracoplasty. Follow-up was available on only four patients – one returning with neuralgia at the tube drainage site and treated by injections of local anaesthetic. We were not happy with these results; there was a high morbidity as we did not directly attack the scarring to lung and chest wall, there was a long hospital stay and a high percentage of patients absconded (*Table 1*). We found that effective non-operative treatment was extremely difficult to maintain and required very forceful supervision. Correct positioning of the intercostal tubes, regular antibiotic administration, management of underwater drainage systems, regular chest X-rays and ensuring sufficient confidence for the patient to overcome his fear of residing in enemy territory, stretched our facilities to the limit. We found it a waste of time to transfer patients out of Mt. Hagen until they were fully recovered. The Highlands' patient tends to deteriorate rapidly once sepsis sets in, for his reaction to illness is to stop eating and stop all forms of activity. Delay also allowed bacterial resistance to build up to our limited supply and range of antibiotics.

In the 12-month period 1 July 1984 to 1 July 1985 we admitted 45 patients with complications of bush thoracotomy. We decided that patients with chronic empyemas not responding over several days to tube drainage would undergo thoracotomy. We eventually got to the stage where we did not insert an intercostal tube but went straight on to thoracotomy, reserving tubes for patients who were toxic when admitted on a non-operating day or when we were waiting for the family to consent to surgery, a decision which involved numerous people who also had to donate the blood for the operation. We tailored the procedures inside the chest to our operative findings. If the disease was caught early then adhesions were broken down, the pyogenic membrane was removed, and after a thorough washout two intercostal tubes were inserted with underwater sealed drainage. However, if a more advanced stage was encountered where there was dense fibrosis of both parietal and visceral pleura, a limited decortication was performed. This consisted of complete mobilization and decortication of all the lobes without removing the parietal pleura. Any alveolar air leaks were left open, only bronchiolar leaks being sutured. Near complete expansion of lung was achieved with the help of the anaesthetist. Occasionally the lower lobe was so firmly adherent to the diaphragm that it was left alone. Entry into the chest was

Table 2 *Period 1 July 1984–1 July 1985*

Diagnosis	Number of patients	Treatment	Length of stay (days)	Deaths	Complications
Empyema					
Acute	1	Aspiration	7	—	Nil
Chronic	29	Tube drainage/thoracotomy	35(17–70)	5 (see *Table 4*)	(see *Table 3*)
Chest pain	4	Physiotherapy/analgesics antibiotics	1, 19, 15, 25	—	Often pain persisted
Wound infection	2	Drainage	3 and 6	—	Nil
Osteomyelitis of the rib	2	Excision/open drainage	24 and 83	—	Pneumothorax (small)
Neuralgia	1	Transthoracic division of intercostal nerves	53	—	Pneumonia
Pneumothorax	1	Antibiotics	5	—	Nil
Absconded	2				
Lost notes	2*				
Refused treatment	1†				

*Probable diagnoses (a) chronic empyema (treated by intercostal tube) and (b) chest pain
†The patient had an empyema but refused thoracotomy

Table 3 *Chronic empyemas in period 1 July 1984–1 July 1985*

Treatment	Number of patients	Length of stay (days)	Deaths (days after admission)	Postoperative complications
Tube drainage alone	9	36(22–58)	1(6)	Nil
Thoracotomies	20			
Debridement only	3	(19, 25 and 42)	Nil	Wound infection (1)
Decortication	17	37(18–70)	4(19, 20, 22 and 28)	Wound infection (1) Unilateral pulmonary oedema (2) Empyema (2) Wound haematoma (1) Stiff shoulder (2) Extrasystoles (1)

One case had a haemoserous pericardial effusion treated by a window. An arrow was found in the chest in only one case, although often cited as the indication for the bush thoracotomy

sometimes hindered by thickened parietal pleura (up to 2 cm thick) in which case sufficient was removed along with one or two ribs to allow access. On one occasion two thoracotomy incisions were made to allow complete mobilization of the underlying lung. All patients were digitalized pre-operatively or during surgery and the decortication operation used on average four units of whole blood. Frequent endotracheal suction was needed during the procedure as we only had single lumen endotracheal tubes and the patients were usually in the full lateral position. They were often left intubated for several hours postoperatively. The patients remained on antibiotics and digoxin while in hospital.

The one acute empyema case in this period was treated by aspiration. Osteomyelitis of the ribs, often associated with a large subcutaneous and intermuscular abscess, was treated by incision, removal of the infected segment and packing. The one patient with definite neuralgia from his bush thoracotomy underwent transthoracic division of four intercostal nerves with a stormy postoperative period complicated by pneumonia – an extrathoracic approach is to be preferred. Our results are shown in *Table 2*. There were three women in this group – two with chronic empyemas and one with a wound infection. There were no children.

There was a large increase in the number of patients during this second 12-month period and in general the patients were much sicker. It is possible that word had spread of our more sympathetic approach so that more patients were coming to us who would have gone to a local health centre or, more likely, died in the village. There did appear to be an increase in tribal fighting during this period, judging from the number of fresh arrow wounds we had to deal with. Four of the patients were referred from peripheral hospitals, and two of them were extremely ill after some months of treatment.

Table 3 outlines our results from managing chronic empyemas in this period. Of our 20 thoracotomies, only 11 had pre-operative intercostal tubes. The four patients dying after decortication all had pre-operative tubes as they were all very ill at the time of admission or had delay in obtaining consent for surgery. One patient underwent open pleural drainage prior to decortication – a large hole was made in the chest wall (partial two rib resection) at the level of the dependent aspect of the empyema and the skin was sutured to the parietal pleura. The hole was large enough to admit the hand for adequate cleaning and packing. Two weeks following open pleural drainage, the patient underwent decortication and, although he developed a haematoma under his latissimus dorsi rotation flap which required drainage and eventual skin grafting, he was discharged very well one month after decortication.

Our complication rate is disappointingly high. We always tried to re-expand the lung on the operating table by increasing the inspiratory pressure gently as early obliteration of the pleural space was a great advantage. The two subsequent cases of unilateral pulmonary oedema responded readily to diuretic therapy. One patient experienced extra systoles for two days without further problems. Two postoperative empyemas developed; one was at the apex which we observed and aspirated until it cleared completely, but one was posterior and burst into a bronchiole rather spectacularly one afternoon. This resolved after tube drainage and no fistula developed. Follow-up was only available on six patients, two complaining of a stiff shoulder on the side of the thoracotomy.

Patients who died in hospital are listed in *Table 4*. All were severely debilitated at the time of admission and deteriorated while in hospital. Case 1 was considered unsalvageable. Case 2 died from a bloody diarrhoea, the cause of which we could not establish and we did not have any metronidazole at that time. Case 3's relatives would only give three units of blood. Case 4 was returned to the ward at night without an endotracheal tube in place and Case 5 had overwhelming sepsis.

Table 5 lists the overall results in patients with complications of bush thoracotomy in comparison with thoracotomies we performed for other reasons during the same period.

Discussion

We were disappointed with the results of our more aggressive surgical approach to the complications of bush thoracotomy in that our mortality rate rose from zero to five deaths when the two 12-month periods are compared. The results reflect an error in the selection of patients for decortication and undue reliance on one type of surgical procedure when others were available[3–6].

We performed open pleural drainage on one patient who was very sick and he improved rapidly. Initially I was wary of this procedure as we were admitting very sick patients with an open pleural drainage hole already established. However, most of the toxicity in these patients was due to secondary pneumonia and sputum retention, problems which were only improved by splinting the mediastinum (closing the hole with dressings or a large tube drain), antibiotics and physiotherapy. Although these empyemas were chronic, there was still some movement in the mediastinum. The empyema could then be treated by the usual underwater tube drainage system. Perhaps some of the toxicity was due to inadequate drainage via the bush thoracotomy hole, especially as the banana leaf dressings tended to prevent pus draining out but not air moving in and out. With open pleural drainage we were able to wash out the pleural cavity every day and then pack it to prevent movement as well as help to eradicate the infection. Following completion of this study, I continued working at Mt. Hagen Hospital for two months and used this procedure more frequently. With resolution of the infection and improvement in lung function, we could go on to decortication if the cavity was large and the patient fit enough, or continue with packing and drainage until healing if the cavity was small or the patient too unwell.

Another surgical procedure which was used only once in this study was thoracoplasty. It proved very useful for the apical residual cavity and may be of value for larger cavities as well, although a more direct attack on the lung seems preferable.

Table 4 *Deaths in chronic empyema patients*

Case	Hospital stay (days)	Particular characteristics of empyema	Treatment	Cause of death
1	6	Large hole in chest wall, heart visible in the depths	Tube drainage	Septicaemia
2	19	Total empyema with osteomyelitis of 2 ribs	Complete visceral decortication 2 days after admission	Bronchospasm/ dysentry ?amoebic ?pseudomembraneous colitis
3	20	Total empyema/severe malaria/massive subcutaneous abscess	Decortication on day 20	Blood loss on the operating table
4	22	Total empyema/refused surgery	Decortication on day 22	Respiratory failure 1 hour postoperatively
5	28	Apical and lateral empyemas/refused surgery	Decortication on day 20	Septicaemia 8 days postoperatively

Table 5 *Comparison of treatments*

Number of cases	Diagnosis	Treatment	Mortality	Mean hospital stay (days)
60	Bush thoracotomy complications			
	40 empyemas	19 ICT alone	1	48
		20 thoracotomy	4	36
		1 refused treatment		
	20 others	Various methods	0	—
37	Trauma*	Thoracotomy†	2	17
4	Other disease	Thoracotomy	1	—

*Of the 37 trauma cases, 33 were arrow wounds, 2 knife wounds, 1 axe wound and 1 stake wound

†18 thoracotomies for trauma involved the lung and 10 consisted of arrow injuries to the heart or major mediastinal vessels

ICT, intercostal tube

As the complications of bush thoracotomy were definitely a problem of young adult males, it was felt important to gain the confidence of this influential group within the villages of the area in question. Very often this would be the first contact with Western hospital practice and we hoped that, if their impressions were favourable, the rest of the tribe would come in earlier when they needed medical attention. The men were very keen on the idea of surgery, whether it was indicated or not, as the discovery of pus or blood in the chest, or better still an arrow, would gain them high prestige and compensation within the village structure. However, consent had to be given by the family and not just by the patient, so that long delays did occur.

Table 5 gives our overall results and compares our death rate with other thoracotomies we performed during the same period. Follow-up rates are very poor as these patients did not stay around once they were discharged but went back to the protection of their own village. From this comparison we also concluded that early thoracotomy, with debridement or decortication, should be reserved for the fitter patients. Once signs of severe sepsis and debility appear then tube drainage should be instituted. Should this fail to resolve the toxicity rapidly, then open pleural drainage is the next step. The need for further surgery depends on the overall improvement in the patient and the extent of resolution. Late decortication is still possible and thoracoplasty may be needed.

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References

1. Sharp P, Cooke R. Chestcutters of the Lagaip. *Med J Aust* 1980; **2:** 707–9.
2. Sharp P. 'Pierced by the arrows of this ghostly world' – A review of arrow wounds in Enga Province. *Papua New Guinea Med J* 1981; **24:** 150–63.
3. Section of Surgery. Discussion on treatment of non-tuberculous empyema. *Proc R Soc Med* 1947; **40:** 645–52.
4. Dieter RA, Pifarre R, Neville WE, Magno M, Jasuja M. Empyema treated with neomycin irrigation and closed-chest drainage. *J Thorac Cardiovasc Surg* 1970; **59:** 496–500.
5. Stafford EG, Clagett OT. Postpneumonectomy empyema neomycin instillation and definitive closure. *J Thorac Cardiovasc Surg* 1972; **63:** 771–5.
6. Rains AJH, Ritchie HD. *Bailey and Love's Short Practice of Surgery*, 18th ed. London: Lewis, 1981: 724–8.

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Prognostic significance of the DNA content of human breast cancer

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The DNA content of paraffin embedded primary tumour tissue has been measured by flow cytometry in 354 patients with operable breast cancer. Tumour ploidy significantly correlated with tumour size, histological grade, and with menopausal status. No significant correlation with oestrogen receptor status or lymph node involvement was found. Patients with diploid cancers had a significantly improved short term survival and disease-free interval (DFI) compared with patients having aneuploid tumours. However, no difference in survival or DFI was shown after longer term follow-up (median 84 months). Multivariate analysis showed no independently significant prognostic value for tumour ploidy. No patient in this study received adjuvant therapy.

Keywords: Breast cancer, tumour ploidy, DNA

It has been suggested that the DNA content of human breast cancer may be of clinical significance as a prognostic factor. A number of breast cancers have an abnormal (aneuploid) DNA content[1,2] and there is evidence from studies using integrating microdensitometry (static cytometry) that patients with diploid carcinomas have an improved prognosis compared to those patients presenting with aneuploid tumours[3,4].

Several investigators have also shown a significant correlation between ploidy and tumour differentiation[1,5] and the degree of lymph node involvement[6]. An association with tumour oestrogen receptor content (ER)[1,2] has been shown, but in most studies this has not achieved statistical significance[1,2,7].

We have undertaken a study to measure the DNA content of paraffin embedded primary tumour tissue by flow cytometry in a series of patients with operable breast cancer. The aims of this study were to investigate the relationship of tumour ploidy to a series of prospectively recorded factors, in a group of patients whose clinical outcome is already known.

Materials and methods

Patients

We followed 354 consecutive female patients with primary operable breast cancer under the care of a single surgeon who had received either simple or subcutaneous mastectomy for a period of 72–132 months (median follow-up 84 months) at the Nottingham City Hospital. None of the patients had received adjuvant systemic therapy. A series of prognostic factors had been recorded at mastectomy on all these patients, including menopausal status, lymph node stage, tumour size, histological grade and tumour ER content.

Patients were classified as being premenopausal if they were still menstruating or had a plasma level of FSH <50 units/l. Lymph node staging was performed at the time of mastectomy using a triple node biopsy technique as previously described[8] and node involvement was judged by histology. Tumour size was recorded as the maximum diameter measured in the fresh mastectomy specimen. Histological grade was assessed by two pathologists (C.W.E. and I.O.E.) using a modification of the Bloom and Richardson Criteria[9]. Tumour tissue ER content was measured by the dextran coated charcoal method[10], a value of >5 fmol/mg cytosol protein being taken as positive.

Follow-up

All patients were treated between January 1974 and April 1979 and were followed up every three months for 18 months, then six monthly for 42 months and annually thereafter. Survival and time to recurrence of disease were recorded.

A prognostic index derived from independently significant factors had been used to stratify patients with different survivals[11]. This index incorporates tumour size, histological grade and lymph node status at mastectomy and has been shown accurately to predict survival in a series of 387 patients. The Nottingham Prognostic Index has been confirmed prospectively on a further series of 320 patients (R. W. Blamey) accurately predicting survival in groups of patients once they have been stratified into 'good' (88 per cent 5 year survival), 'moderate' (69 per cent 5 year survival) and 'poor' (22 per cent 5 year survival) prognostic groups. The patients in this report have been allocated to these prognostic groups, as determined by their prognostic index score, and this has been compared with tumour ploidy.

Flow cytometry

The presence of tumour in paraffin embedded tissue was confirmed histologically and tissue sections containing >10 per cent of cancer cells were selected for DNA analysis.

Cell nuclei were obtained from two 30 μm sections of primary tumour after dewaxing, rehydration and pepsin digestion. The nuclei were then stained with a stoichiometric DNA specific fluorescent stain, diamidino-2-phenylindole dihydrochloride (DAPI)[12]. A DNA index was calculated from histograms obtained by measuring the nuclear fluorescence of a minimum of 20000 nuclei using a FACS Analyser. The DNA index of each tumour is derived from a ratio of the G_0/G_1 DNA content of the nuclei of tumour tissue compared to the DNA content of G_0/G_1 nuclei of normal (diploid) cells. By definition diploid cells have a DNA index of 1·0[13].

We have assessed the value of internal diploid standards with this technique but neither fresh nor formalin fixed human diploid tissue gave consistent ratios between the internal standard and the diploid G_1 peak of the formalin fixed paraffin embedded tissue. This had previously been noted by Hedley[12]. Therefore no internal diploid standard was used in this study. In previous studies[14] we have invariably identified a population of cells with a diploid DNA content in fresh tumour tissue compared with an internal diploid standard.

Statistics

Actuarial analysis using Mantel's Life Table Method was used to determine the influence of the DNA content of tumours on survival and disease free interval (DFI). Correlations between tumour ploidy and size, grade, lymph node stage, ER content, menopausal status and prognostic groups were examined by χ^2 analysis. Cox multivariate analysis was used to determine the independent significance of tumour ploidy compared with patient survival.

Results

Of the breast cancers analysed, 141 (40 per cent) had a DNA index of 1·0 (diploid); the remaining 213 tumours were aneuploid. The coefficient of variation had a range of

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Table 1 *Tumour size compared with DNA content (350 patients)*

	Tumour size (cm)		
	≤2·0	2·1–5·0	>5·0
Diploid (139)	67	58	14
Aneuploid (211)	69	111	31
Total	136	169	45

$\chi^2=8·63$, 2 d.f., $P<0·02$

Table 2 *Tumour grade compared with DNA content (348 patients)*

	Grade of differentiation		
	1 (Well)	2 (Moderate)	3 (Poor)
Diploid (138)	46	55	37
Aneuploid (210)	14	67	129
Total	60	122	166

$\chi^2=56·77$, 2 d.f., $P<0·001$

Table 3 *Menopausal status compared with DNA content (348 patients)*

	Premenopausal	Postmenopausal
Diploid (139)	64	75
Aneuploid (209)	59	150
Total	123	225

$\chi^2=11·60$, 1 d.f., $P<0·01$

Table 4 *Prognostic groups compared with DNA content (350 patients)*

	Prognostic groups		
	Good	Moderate	Poor
Diploid (139)	55	62	22
Aneuploid (211)	25	125	61
Total	80	187	83

$\chi^2=37·58$, 2 d.f., $P<0·001$

4·9–8·7 per cent with a mean of 6·6 per cent. We analysed 96 of the tumours on at least two occasions with a correlation of 88/96 (92 per cent) for ploidy status.

Tumour size

A significant correlation has been found between tumour ploidy and size in the 350 patients in whom accurate tumour measurements were available at mastectomy. Diploid tumours were associated with smaller tumour size (*Table 1*).

Histological grade

Four patients with non-invasive carcinomas who underwent mastectomy for *in situ* change have been excluded from this analysis. In the remaining 348 patients a strong correlation exists between ploidy and grade, diploid tumours being associated with the better histological grades (*Table 2*).

Lymph node status

Lymph node status was available in 350 patients. An association was found between lymph node status and tumour ploidy which failed to reach statistical significance ($\chi^2=3·81$ (1 d.f.)), 57/139 (41 per cent) patients with diploid tumours having lymph node involvement compared with 109/211 (51·6 per cent) of node positive patients with aneuploid tumours. No correlation was found between ploidy and the degree of lymph node involvement.

Menopausal status

Of 348 patients in whom menopausal status was recorded, 123 (35 per cent) were premenopausal. A significant correlation was found between menopausal status and tumour ploidy, the premenopausal were significantly more likely to have diploid cancers than postmenopausal patients (*Table 3*).

ER status

The ER content had been measured in the primary tumour tissue of 312 patients, 185 (57 per cent) were ER positive. Of the diploid tumours, 75/118 (63·6 per cent) were ER positive compared with 110/194 (56·7 per cent) of aneuploid cancers. Although there was a trend for diploid cancers to be ER positive this difference failed to reach statistical significance ($\chi^2=1·43$, 1 d.f.).

Prognostic groups

It was possible to allocate 350 patients to prognostic groups using the Nottingham Prognostic Index (*Table 4*). A strong correlation was identified between ploidy and prognostic grouping, with diploid cancers more frequently associated with the better prognostic groups.

Survival

No overall significant difference in survival was found between patients presenting with diploid or aneuploid primary tumours after a median follow-up of 84 months (*Figure 1*). However, when patient survival was analysed at 30 months after mastectomy a significant advantage for diploid cancers exists ($\chi^2=9·07$, 1 d.f., $P<0·01$).

The distribution of tumours grouped by DNA index is shown in *Table 5*. The number of tumours with a DNA index of between 1·05 and 1·2 or >1·9 is small and these patients have a similar survival to that of patients with diploid tumours (DNA index 1·00). However, the majority of patients with aneuploid cancers have a DNA index of between 1·21 and 1·90 and these patients

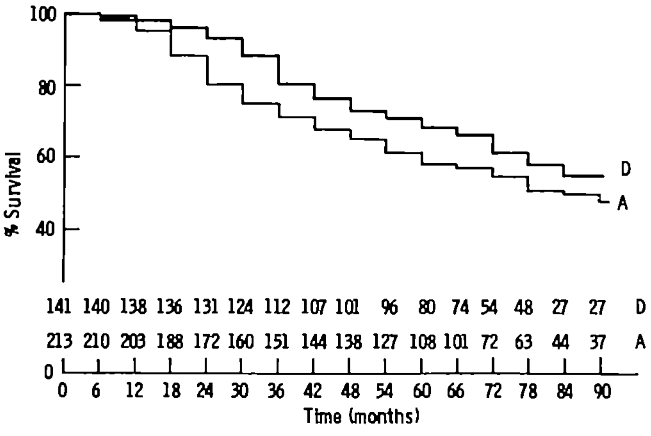

Figure 1 *The correlation of DNA content with survival: all cases.* $\chi^2=3·30$, *1 d.f., n.s. D, diploid; A, aneuploid*

Table 5 *DNA index of 354 breast cancers*

DNA index	Number
1·0	141 (Diploid)
1·05–1·2	8 ('Near diploid')
>1·2–1·9	166
>1·9–2·1	20 ('Tetraploid')
>2·1	19

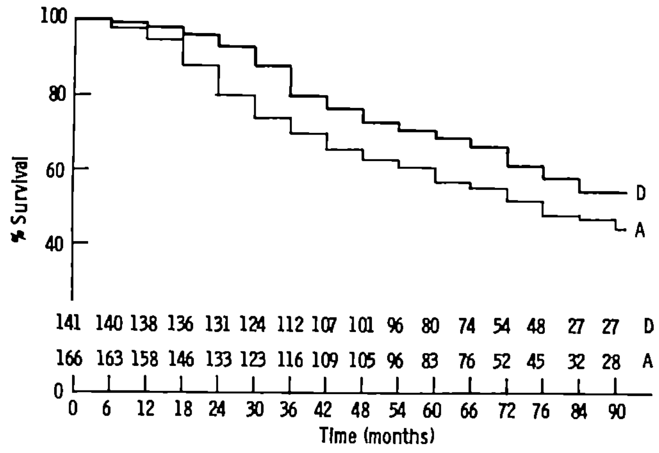

Figure 2 *Comparison of survival of patients with tumours with a DNA index of 1·0 (diploid) with those with a DNA index of 1·21–1·90, (47 patients with DNA index between 1·05 and 1·2 or >1·9 have been excluded, see* (Table 5). $\chi^2=4{\cdot}81$, *1 d.f.,* P<0·05. *D, diploid; A, DNA index 1·21–1·9*

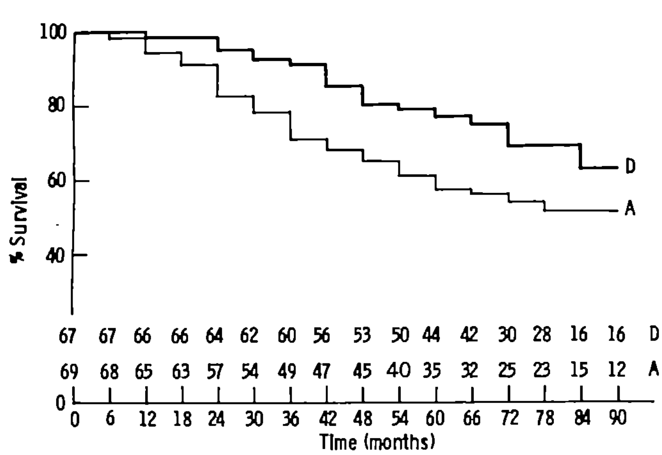

Figure 3 *Tumour size* $\leqslant$*2 cm: the correlation of DNA content with survival (136 patients).* $\chi^2=4{\cdot}17$, *1 d.f.,* P<0·05. *D, diploid; A, aneuploid*

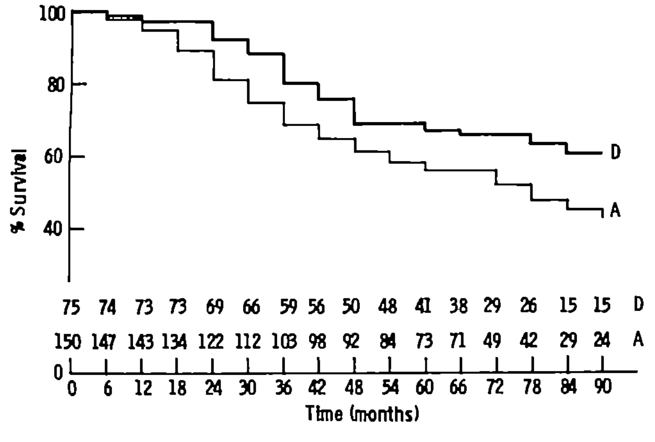

Figure 4 *Postmenopausal: the correlation of DNA content with survival (225 patients).* $\chi^2=3{\cdot}99$ *1 d.f.,* P<0·05. *D, diploid; A, aneuploid*

have a significantly worse survival than patients with diploid cancer for the whole of the follow-up period (*Figure 2*).

Analysis of patient survival has been performed after subgrouping the patients for tumour size, histological grade, lymph node stage, menopausal status and ER content. Patients with diploid cancers were shown to have a significant survival advantage over patients with aneuploid tumours if they presented with cancers $\leqslant$2 cm in size (*Figure 3*) or if they were postmenopausal (*Figure 4*).

A Cox multivariate analysis was performed on those factors known to be independently and significantly contributing towards patient survival (tumour size, grade and lymph node stage) and tumour ploidy (*Table 6*). The DNA index was not shown to be a significant independent prognostic factor. The Cox analysis was repeated using the subgroups of aneuploid tumours previously described (*Table 5*); no independent prognostic significance was found for any subgroup.

Disease free interval

No significant overall difference has been found between patients with diploid and aneuploid tumours (*Figure 5*). However, when those patients whose disease recurs within 30 months of mastectomy are examined there is a significant difference, more patients with aneuploid cancers having a recurrence ($\chi^2=6{\cdot}036$, 1 d.f., $P<0{\cdot}01$). The probability of recurrence is significantly greater in those patients with a DNA index of between 1·21 and 1·90 and this greater risk of recurrence is noted throughout the follow-up period.

Discussion

Previous reports measuring Feulgen acid hydrolysis of DNA by integrating microdensitometry have suggested that the ploidy of tumour tissue in patients with primary breast cancer may be of prognostic value. The accuracy of flow cytometric analysis is improved by its ability to measure large numbers of nuclei using stoichiometric DNA specific stains. We have undertaken studies[14] which confirm that the DNA index in fresh tumour tissue, using Mithramycin and an internal diploid standard, correlates well with results obtained from the same primary tumours, two years after fixation, using DAPI staining.

In this study the DNA content has been measured in a large series of patients with primary breast carcinoma treated initially by surgery alone, all of whom have been followed for a minimum of six years after mastectomy. We have shown that patients with diploid breast cancers have an improved short term survival compared with patients with aneuploid tumours. However, with

Table 6 *Values of β and Z obtained for each factor from Cox analysis*

	β value	Z value
Tumour size	0·12	2·00*
Grade	0·80	6·20**
Lymph node stage	0·64	6·51**
DNA index	−0·29	−1·57

*$P<0{\cdot}05$, **$P<0{\cdot}001$

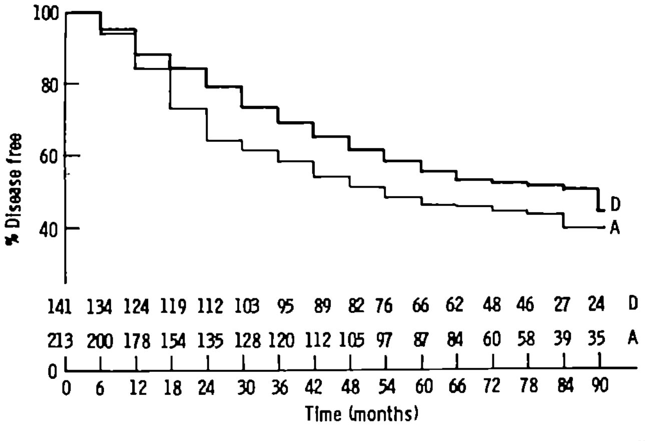

Figure 5 *The correlation of DNA content with disease recurrence: all cases.* $\chi^2=2{\cdot}58$, *1 d.f., n.s. D, diploid; A, aneuploid*

longer follow-up no significant survival difference can be identified between these two groups of patients. This agrees with the findings of previous reports which showed an improved survival for patients with diploid tumours after short term follow-up.

Auer has previously described the distribution of DNA content of tumours in patients dying within two years of diagnosis and those alive 15 years after diagnosis, classifying the tumours into four types[4]. When the patients in our series were subgrouped by DNA index distribution, similar to Auer's four types, we have been able to show that patients with tumours with a DNA index of 1·0, 1·05–1·2 and >1·9 survive at similar rates. There is however a large group of patients with a DNA index of between 1·21 and 1·90 (similar to Auer's Group III) who have a significantly worse survival than patients with any other DNA index.

The correlations between DFI and ploidy exactly mirror those of survival in our series and confirm Hedley's finding of an early DFI advantage for diploid cancers[6]. However, unlike Hedley's report, none of the patients in this series received any form of adjuvant therapy and therefore the observed differences in DFI cannot be accounted for by an increased sensitivity of diploid cancers to chemotherapeutic agents.

There are in this series significant correlations between diploid cancers, good histological differentation and small tumour size. These correlations are reflected in a significant association between ploidy status and the Nottingham Prognostic Index.

Patients with aneuploid tumours have a higher rate of early recurrence and early death from their carcinoma than patients with diploid tumours. With longer follow-up no significant survival difference was identified between all patients with diploid carcinomas and all patients with aneuploid carcinomas. However, it was possible to identify a large subgroup of patients with a DNA index between 1·21 and 1·9 who have a significantly worse prognosis for the whole of the follow-up period.

Nevertheless, multivariate analysis failed to show a significant independent prognostic value for tumour ploidy and it is possible that the strong association between ploidy and histological grade may account for the survival differences noted in this study.

References

1. Olszewski W, Darzynkiewicz Z, Rosen PP, Schwartz M, Melamed M. Flow cytometry of breast carcinoma 1. Relation of DNA ploidy level to histology and estrogen receptor. *Cancer* 1981; **48**: 980–4.
2. Kute TE, Muss HB, Anderson D *et al.* Relationship of steroid receptor, cell kinetics and clinical status in patients with breast cancer. *Cancer Research* 1981; **41**: 3524–9.
3. Atkin NB. Modal deoxyribonucleic acid value and survival in carcinoma of the breast. *Br Med J* 1972; **i**: 271–2.
4. Auer G, Eriksson E, Azavedd E, Caspersson T, Wallgren A. Prognostic significance of nuclear DNA content in mammary adenocarcinomas in humans. *Cancer Research* 1984; **44**: 394–6.
5. Tavares AS. Ploidy and histological types of mammary carcinoma. *Eur J Cancer* 1986; **3**: 449–55.
6. Hedley DW, Rugg CA, Ng ABP, Taylor IW. Influence of cellular DNA content on disease free survival of stage II breast cancer patients. *Cancer Research* 1984; **44**: 5395–8.
7. Horsfall DJ, Tilley WD, Orell SR, Marshall VR, Cant EL. Relationship between ploidy and steroid hormone receptors in primary invasive cancer. *Br J Cancer* 1986; **53**: 23–8.
8. Blamey RW, Bishop HM, Blake JRS *et al.* Relationship between primary breast tumour receptor status and patient survival. *Cancer* 1980; **46**: 2765–9.
9. Elston CW, Gresham GA, Rao GS *et al.* The Cancer Research Campaign (King's/Cambridge) trial for early breast cancer: clinico-pathological aspects. *Br J Cancer* 1982; **45**: 655–69.
10. Maynard PV, Griffiths K. Clinical pathological and biochemical aspects of the oestrogen receptor in primary human breast cancer. In: King RJB, ed. *Steroid Receptor Assays in Human Breast Tumours: Methodological and Clinical Aspects.* Cardiff, UK: Alpha Omega Alpha Publishing Co, 1978.
11. Haybittle JL, Blamey RW, Elston CW *et al.* A prognostic index for primary breast cancer. *Br J Cancer* 1982; **45**: 361–6.
12. Hedley DW, Friedlander ML, Taylor IW, Rugg CA, Musgrove EA. Method for analysis of cellular DNA content of paraffin embedded pathological material of using flow cytometry. *J Histochem Cytochem* 1983; **31**: 1333–5.
13. Hiddemann W, Schumann J, Andreef M *et al.* Convention on nomenclature for DNA cytometry. *Cytometry* 1984; **5**: 445–6.
14. Owainati A, Robins RA, Hinton CP *et al.* Tumour aneuploidy, prognostic parameters and survival in primary breast cancer. *Br J Cancer* 1987 (in press).

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The intragastric balloon: a novel idea proved ineffective

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Twelve grossly obese patients who weighed 121 ± 22 kg (mean ± s.d.) had a free-floating 600 ml spherical intragastric balloon inserted per oesophagus and have been followed for 12–24 months. Nine patients lost up to 21 kg (11 ± 6·4 kg) over 3 months after which they reached a plateau and then regained weight so that by 1 year only one patient had maintained her weight loss. Three patients could not tolerate the balloon owing to complete reflex inhibition of gastric emptying. Such marginal and temporary weight loss is of no value in the treatment of gross obesity.

Keywords: Obesity, intragastric balloon

Obesity operations are not without hazard and are only acceptable because of the consistently poor results obtained by more conservative treatments. Such operations can only be justified in grossly obese patients. It has been suggested that an intragastric balloon can reduce appetite, food intake and thence weight. If so, the intragastric balloon has several advantages compared with surgery, being less invasive and reversible, yet still incapable of being tampered with by the patient. Unlike jaw wiring, it is not a cosmetic embarrassment and allows the patient to eat a normal diet. There have been several optimistic preliminary reports but no data to show that the balloon is effective.

Neiben and Harboe[1] were the first to describe the therapeutic use of an intragastric balloon and their patients achieved encouraging weight loss (2–5 kg in 7–21 days). Similar weight loss was achieved by others in volunteers[2,3] and patients[4,5] although the success was short lived as they were using latex balloons which failed in a few weeks. Percival[5] uses balloons attached to a nasal cannula which can be removed and replaced as often as necessary and has inserted them into 108 patients since 1980 but has yet to publish his figures for weight loss. Taylor[6] has, like us, overcome the problem of balloon failure by using balloons made of silicone elastomer and reports encouraging early weight loss but with only 3 months follow-up.

We have developed a method of introducing a free-floating balloon which is sufficiently robust, and have treated 12 grossly obese patients who have now been followed for long enough to comment on its safety and efficacy.

Patients and methods

Patients

Ten women and two men, aged 35 ± 7·7 years, have had an intragastric balloon (*Table 1*). Average weight was 121 ± 7·7 kg and body mass index (BMI) 44 ± 6·3 kg/m^2. None had any history of gastrointestinal disease. All fulfilled our strict criteria for obesity surgery being less than 50 years old, more than 50 per cent overweight (BMI $> 35\ kg/m^2$) and having failed conventional treatment. We felt it was inappropriate to relax these criteria for an experimental procedure.

Resting metabolic rate was measured by indirect calorimetry in 10 of these patients using a ventilated hood apparatus. Oxygen consumption at rest was 281 ± 52 ml/min. This implies a daily expenditure of around 2330 kcal (assuming the energy equivalent of oxygen is 4·8 kcal/l and that overall daily energy expenditure is 1·2 times greater than resting expenditure). This figure corresponds to the energy intake necessary to maintain their weight and compares with an intake of 2572 kcal estimated from the dietary history.

Materials and methods

Inflatable balloons made of silicone elastomer have proved serviceable as breast augmentation prostheses where they have proved durable and relatively non-allergenic. The balloons incorporate a 'flutter' valve and are inflated by a narrow bore 'fill-tube' inserted through the valve. After inflating the balloon with saline the fill-tube is withdrawn and the valve seals. We developed our technique of introducing the balloon in greyhound experiments and found a 600 ml balloon, spherical and considerably larger than the breast prostheses, produced weight loss without distress or ill health. Smaller balloons were ineffective in the dogs and so a 600 ml balloon was used in the patient study.

The fill-tube was inserted through the valve and the empty balloon was rolled tightly around it before loading into a length of semi-rigid polytetrafluoroethylene (PTFE) tubing. Within this outer tube was a hollow piston, bored to accept the fill-tube (*Figure 1*). Under light general anaesthesia, the patient was endoscoped to exclude upper gastrointestinal pathology. The introducer was passed per oesophagus under fluoroscopic guidance, until its end was seen to be just into the stomach, then the piston was advanced pushing the balloon out into the stomach, still with the fill-tube in place through the valve. Conray 280 (May and Baker), 50 ml, was injected to identify the balloon clearly (*Figure 2*). The balloon was then inflated to a total of 600 ml with physiological saline. Briskly withdrawing the fill-tube released the balloon.

Free fluids were allowed immediately and patients ate normally the following day. All were observed for at least 48 h as part of the protocol but this was unnecessary for the majority. They were advised to eat meals rather than nibble, avoid high energy/low bulk foods such as chocolate, and to regard the balloon as an aid to dieting not absolving them from any effort of their own.

Deflation of the balloons was most easily achieved by direct percutaneous puncture and aspiration under fluoroscopic guidance. Usually the balloon could be completely aspirated and allowed to pass per rectum.

Informed consent was obtained and the protocol was approved by the Ethical Committee of St. George's Hospital.

Results

The insertion procedure was successful in all patients and was well tolerated.

Postoperative course

All the patients were aware of the balloon. There was an uncomfortable heaviness after only a few mouthfuls of food and a disinclination to eat between meals. Seven patients were discharged from hospital within 3 days of inserting the balloon, although three of these had abdominal cramps for several days. Two further patients were more distressed and for 7–10 days were unable to eat solid food without vomiting. The cramps were relieved by lying on the left side, suggesting they were due to the balloon stimulating the antrum.

Three patients (nos. 3, 10 and 11) had severe vomiting and cramps and could not maintain fluid and electrolyte balance. A nasogastric tube partially relieved the symptoms but from the volume aspirated it was clear the stomach was not emptying. Barium studies showed the balloon was not impacted in the

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Table 1 *Patients, weight loss and outcome*

Patient	Weight (kg)	Postoperative course	Weight loss 1 month	3 months	6 months	12 months	Comments
1	163	Vomited 10 days	8	10	8	—	Punctured at 8 months
2	111	—	9	14	16	0	Punctured at 12 months
3	106	Gastric retention	—	—	—	—	Puncutred at 18 days
4	110	—	7	11	14	20	Loss of 23 kg at 2 years
5	127	—	12	21	19	19	Loss of 11 kg at 2 years
6	149	—	6	17	11	0	Still inflated at 12 months
7	138	—	8	11	12	6	Punctured at 16 months
8	93	Vomiting 7 days	7	8	8	—	Punctured at 6 months
9	117	—	5	6	6	0	Failed follow-up
10	90	Gastric retention	—	—	—	—	Punctured at 18 days
11	131	Gastric retention	—	—	—	—	Punctured at 16 days
12	120	—	1	0	0	—	Punctured at 6 months

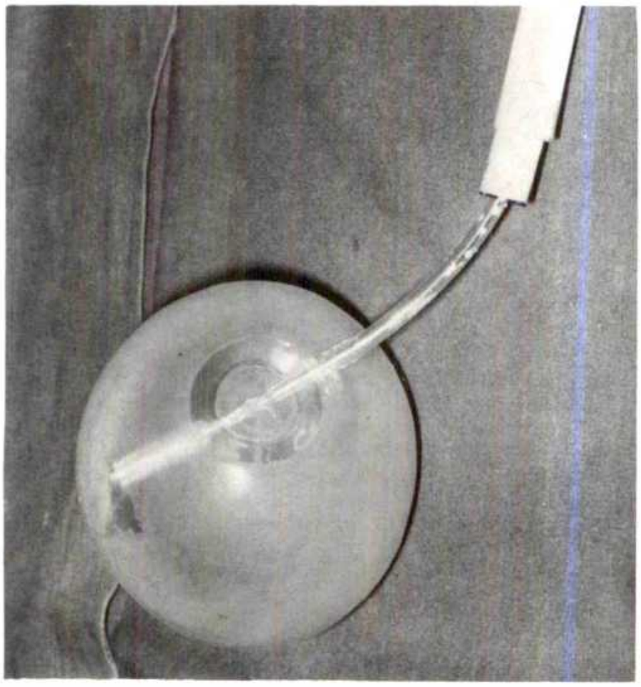

Figure 1 *A 600 ml silicone balloon being prepared for loading into the introducer*

antrum; contrast passed the balloon into the antrum yet the pylorus remained closed even after several hours (*Figure 3*). A gastroscope passed easily into the duodenum confirming there was no mechanical obstruction. After two weeks without improvement, the balloon was punctured and recovery was immediate.

Weight loss

The nine patients who were able to tolerate the balloon lost a mean 11 ± 6·4 kg in 3 months. This weight loss (21 kg in one patient) was a noticeable improvement although the patients were still obese. All patients commented they felt less hungry between meals and were satisfied with smaller quantities. By 3 months, however, this sensation was less marked and weight loss reached a plateau. Only one patient (no. 4), with considerable effort, has managed to continue losing weight and at 2 years weighs 87 kg (BMI 32 kg/m^2). One patient has regained weight to 11 kg below his starting weight and all the rest have reached or even exceeded their initial weight.

Complications

No serious complications have occurred. No patient developed a peptic ulcer, despite this being a known complication of

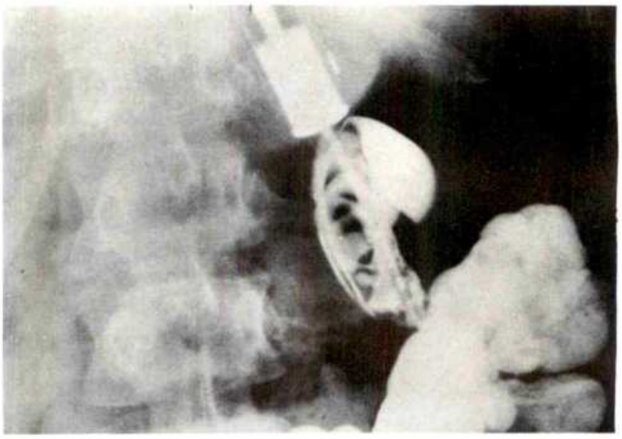

Figure 2 *The balloon has been pushed out of the introducer by the piston, 50 ml 'Conray 280' has been injected down the fill-tube and the balloon is just beginning to inflate (the transverse colon still contains barium sulphate from a study several days earlier)*

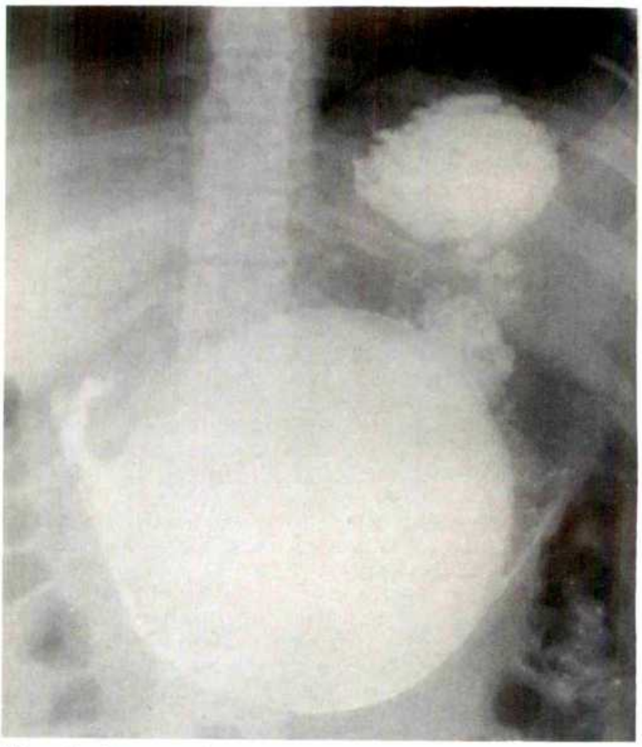

Figure 3 *Barium meal on patient no. 3 shows a balloon* in situ. *Contrast passes the balloon and fills the antrum yet the pylorus remains closed. No barium has left the stomach even after 90 min*

trichobezoars[7], and experimental evidence that intragastric balloons cause hypergastrinaemia[8]. We measured fasting gastrin levels which were normal and did not increase after the balloon was inserted.

Most patients never felt quite comfortable; while this was acceptable when they were losing weight they became disheartened when they stopped losing and five have now had the balloon deflated. Four patients complained of foul eructation and all patients had a large residual volume in the stomach as evidenced by the fluid level on plain abdominal X-ray.

Balloon deflation

No balloon had deflated spontaneously at the 1 year review, although one has since. The balloons maintained their volume; when they were eventually punctured nearly 600 ml could be aspirated. Eight balloons have been let down by us, three for gastric retention and five at 8–16 months when the balloon was no longer effective. All but one has passed per rectum, usually within 2 weeks. In this one patient, who was sensitive to iodine, we made the mistake of using barium sulphate instead of water-soluble contrast to identify the balloon. The barium set and 6 months after deflation the balloon was still in the stomach. Although it was causing the patient no symptoms the balloon was removed by gastrotomy at her request.

Discussion

The intragastric balloon was worth investigating as it offered the chance of producing weight loss without exchanging the hazards of obesity for the considerable hazards of jejunoileal bypass[9,10] or gastric surgery[11–13]. It was a plausible idea as gastric distension has been recognized as a satiety mechanism in the experimental animal for many years [14–17] and trichobezoars and phytobezoars can present as weight loss in an otherwise healthy subject[7].

The problem of balloon failure was overcome by using a silicone prosthesis. Early weight loss was encouraging, and comparable with the results of other non-operative treatments for obesity. Nine patients lost 1–21 kg in 3 months and no serious complication has occurred even after 1 year. Like other authors, we were able to produce a feeling of early satiety in our patients. While this is most likely to be due to the stimulation of gastric stretch receptors early in the course of a meal, the large fermenting gastric residue may have contributed to the loss of appetite, as it does when truncal vagotomy is performed for obesity[18]. In three of the twelve patients this reflex inhibition of gastric emptying was complete. A smaller balloon may be better tolerated but our animal experiments suggested that a smaller balloon was less effective.

It is disappointing that the satiety effect of the balloon only lasted 3 months. The weight was maintained at the new level for a few months more by some patients with difficulty. At 1 year almost all our patients had regained or even exceeded their starting weight. One had lost 21 kg by 3 months but after 2 years has fallen back to 11 kg and is slowly gaining. Only one patient has persevered and by dieting has reached 87 kg after 2 years. It is fair to say that almost any treatment programme, administered with enthusiasm, can produce results as good as this.

For our grossly obese patients, such marginal and temporary weight loss is insufficient to be of benefit and the intragastric balloon must be considered ineffective. However our limited experience, with that reported by others, suggests the intragastric balloon may be safe enough for use in patients in whom 10–20 kg weight loss may be desirable yet who would not be considered for obesity surgery, for example the less than grossly obese, the older and the medically unfit patients. Such limited weight loss may also be of disproportionate benefit in patients with diseases aggravated by obesity. Even so the balloon will be of little value unless its effect can be prolonged, or at least the weight loss maintained beyond 6 months. The only situation in which the temporary nature of the effect would not be a disadvantage would be in the use of the balloon to induce weight loss in patients awaiting elective surgery, including obesity surgery.

Acknowledgements

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References

1. Neiben OG, Harboe H. Intragastric balloon as an artificial bezoar for treatment of obesity. *Lancet* 1982; **i**: 198–9.
2. Hennig AE. Ambulante Gewichtsredukhon durch einen intragastral applizietzn Ballon erste Erfahrungen. *Inn Med* 1979; **6**: 149–52.
3. Frimberger E, Kuhner W, Weingart J, Ottenjann R. Intragastraler Appetit-Depressor-Ballon. *Munch Med Wschr* 1982; **124**: 61–2.
4. Taylor TV, Pullen BR. Initial experience with a free.floating intragastric balloon in the treatment of morbid obesity. *Gut* 1983; **24**: A979.
5. Percival WL. The ‘balloon diet’: a noninvasive treatment for morbid obesity. preliminary report on 108 patients. *Can J Surg* 1984; **27**: 135–6.
6. Durrans D, Taylor TV, Pullen BR, Rose P. Intragastric balloon: Short term solution to a long term problem. *J R Coll Surg Edinb* 1985; **30**: 369–71.
7. Debakey M, Ochsner A. Bezoars and concretions. *Surgery* 1938; **4**: 934–63 and 1939; **5**: 132–60.
8. Feurle GE, Tisheirek K, Helmstaedter V. Intragastric balloons causing gastric hypertrophy, G cell hyperplasia and raised serum gastrin levels in rats. *Lancet* 1982; **ii**: 386.
9. McFarland RJ, Gazet J-C, Pilkington TRE. A thirteen year review of jejunoileal bypass. *Br J Surg* 1985; **72**: 81–7.
10. Hocking MP, Duerson MC, O’Leary JP, Woodward ER. Jejunoileal bypass for morbid obesity: late follow up in 100 cases. *New Engl J Med* 1983; **308**: 995–8.
11. Griffen WO. Gastric bypass for morbid obesity. *Surg Clin N Am* 1979; **59**: 1103–12.
12. Buckwalter JA, Herbst CA. Gastric partition for morbid obesity: greater curvature gastroplasty or gastrogastrostomy. *World J Surg* 1982; **6**: 403–11.
13. Crowley LV, Seay J, Mullin G. Late effects of gastric bypass for obesity. *Am J Gastroenterol* 1984; **79**: 850–60.
14. Janowitz HD, Grossman MI. Some factors affecting the food intake of normal dogs and dogs with oesophagostomy and gastric fistula. *Am J Physiol* 1949; **159**: 143–8.
15. Share I, Martyniuk E, Grossman MI. Effect of prolonged intragastric feeding in oral food intake in dogs. *Am J Physiol* 1952; **159**: 229–35.
16. Davis JD, Campbell CS. Peripheral control of meal size in the rat: effect of sham feeding on meal size and drinking water. *J Comp Physiol Psychol* 1973; **83**: 379–87.
17. Deutsch JA, Young WG, Kalogeris TJ. The stomach signals satiety. *Science* 1978; **201**: 165–7.
18. Kral JG. Vagotomy for treatment of severe obesity. *Lancet* 1978; **i**: 307–8.

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Chloroquine administration for malaria suppression after abdominal surgery

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Administration of chloroquine after major surgery is indicated in malaria endemic areas. In emergencies it is commonly administered parenterally after the operation. The present study, undertaken at St. Francis Hospital, Ifakara (Kilombero District), Tanzania, compared plasma chloroquine levels after oral and subcutaneous administration of 300 mg of chloroquine base in 14 patients after abdominal, non-bowel-resective surgery and in 12 controls. There were no significant differences in the plasma chloroquine levels of all groups, and the chloroquine concentrations reached suppressive levels for at least 3 days (>0·1 nmol/ml). Oral administration was well tolerated in both patients and controls. In all areas where the Plasmodium *strains are still sensitive to chloroquine and where parenteral chloroquine may not be easily available, oral chloroquine represents a cheap, easy and safe alternative for postoperative prophylactic malaria suppression. It can be applied after abdominal non-bowel-resective emergency surgery.*

Keywords: Chloroquine, abdominal surgery, postoperative malaria

Malaria is a frequent postoperative concomitant disease in the tropics. In endemic areas, about 10 per cent of all operated caucasians suffer from postoperative malarial attacks[1] and about 50 per cent of all postoperative fevers in African patients are attributed to malaria[2]. An efficient postoperative malaria suppression is therefore indicated to avoid malaria recrudescence in the postoperative phase; to prevent malaria induced by blood transfusions and to exclude malaria in the differential diagnosis of postoperative fever. In elective surgery the anti-malarial drugs can easily be given orally 12 h before anaesthesia. Yet, as many operations are emergencies, the anti-malarial drugs can only be administered either parenterally or orally in the postoperative phase. In countries where malaria is endemic, parenteral chloroquine is often not available and, if at all, very expensive. In addition, parenteral administration is usually much more complicated (material, sterility, storage, injection) and not without risk[3]; the peroral route of administration is preferable. There is very limited information on whether peroral malaria suppression is possible after abdominal surgery and whether it is as efficient as the parenteral administration. The present study compared the plasma levels of chloroquine administered orally or parenterally after non-bowel-resective abdominal surgery.

Patients and methods

The study was performed at the St. Francis Designated District Hospital in Ifakara (Kilombero District, Morogoro Region), Tanzania. Ifakara is a rural town and is situated in the Kilombero river plain 350 km south-west of Dar-es-Salaam at an altitude of 250 m. The area is well known to be holo-endemic for malaria[4].

Patients with a postoperative paralytic phase for at least 12–24 h after abdominal emergency operations for diseases not requiring bowel resection (Caesarean section, 5; salpingectomy, 4; sigmoid volvulus, 3; adhesions, 1; truncal vagotomy, 1) were randomly assigned to the following two prophylactic anti-malarial treatment groups. Group A: eight patients received two tablets (300 mg) of chloroquine-base (Resochin® Bayer) orally with 50 cm^3 water. Group B: six patients were injected with 300 mg of chloroquine-base (Resochin®, Bayer) subcutaneously in two doses of 150 mg (5 cm^3) laterally in each thigh. The corresponding two control groups (groups C and D, six each) were selected among patients admitted to the St. Francis Hospital with fractures or for small extra-abdominal operations with locoregional anaesthesia (e.g. hernia, hydrocele). Thick smears were made in all cases of postoperative fever. Venous blood was drawn by EDTA vacutainers before and 24 h, 72 h and 7 days after the administration of chloroquine-base, which occurred 30–60 min postoperatively. The blood was subsequently centrifuged within the next 30 min. The plasma was frozen (−20°C) and shipped on dry ice to Basle, Switzerland. The plasma chloroquine levels were measured by high performance thin layer chromatography (HPTLC)[5], at the Swiss Tropical Institute.

Results

Groups A and B and the controls were comparable with regard to age, sex and weight as well as type of operation for A and B. The median plasma chloroquine levels are shown in *Table 1* and *Figure 1*. There was neither a significant difference in the plasma chloroquine levels between patient groups A and B, i.e. the oral and subcutaneous route, nor between groups A and B and the 12 controls. All patients reached plasma chloroquine levels above the level required for *in vivo* suppression of chloroquine sensitive *Plasmodium falciparum* strains[6] (>0·1 nmol/ml, *Table 1*) during the first 3 postoperative days, when 90 per cent of postoperative malarial attacks are reported[2]. None of the patients had a positive blood smear for malaria after 24 h, 72 h or 7 days.

The peroral chloroquine was well tolerated, in all groups. No nausea, vomiting or other gastrointestinal disturbances were recorded. Initial plasma chloroquine levels (*Table 1*) were present in most patients, which may be explained by the wide-spread use of chloroquine in Tanzania, together with the long half life of chloroquine[6].

Discussion

Earlier reports showed that nearly half of all postoperative fevers are due to malaria[2]. Postoperative prophylactic malaria suppression seems extremely useful to avoid malaria recrudescence during the postoperative phase, to prevent malaria induced by blood transfusions and to exclude malaria in the differential diagnosis of postoperative fever. The present study revealed that oral chloroquine base is well absorbed and well tolerated after non-bowel-resective abdominal surgery. Plasma chloroquine levels after oral administration are comparable with the subcutaneous administration. Oral

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Table 1 *Plasma chloroquine levels (nmol/ml) of patients receiving postoperative malaria prophylaxis (300 mg chloroquine base) orally or parenterally (s.c.) after abdominal surgery and controls. Medians (±95 per cent confidence limits) are represented*

Group	Patients	*n*	Pre-operative	24 h	72 h	7 days
A	Oral administration	8	0·025 (0·005–0·3)	0·175 (0·11–1·17)	0·120 (0·03–0·17)	0·07 (0·04–0·15)
B	Parenteral administration	6	0·02 (0·00–0·06)	0·310 (0·17–1·46)	0·170 (0·08–0·35)	0·05 (0·00–0·8)
C	Controls to A	6	0·035 (0·004–0·16)	0·155 (0·05–0·24)	0·07 (0·03–0·12)	0·03 (0·02–0·05)
D	Controls to B	6	0·06 (0·008–0·12)	0·240 (0·10–0·39)	0·180 (0·08–0·23)	0·115 (0·04–0·24)

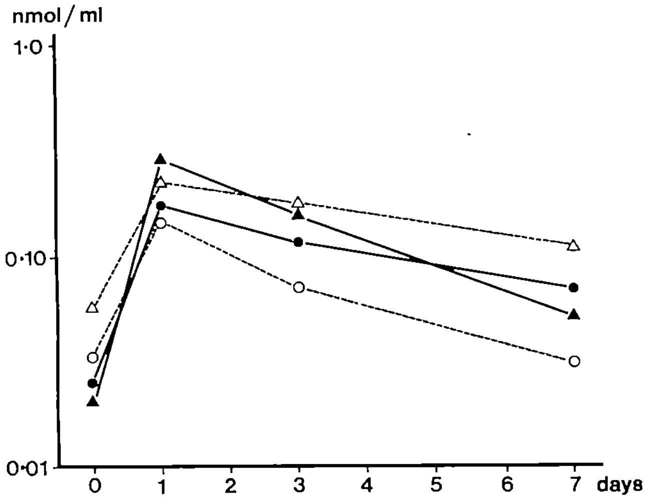

Figure 1 *Median plasma chloroquine levels (nmol per ml) after the administration of 300 mg chloroquine base in patients (non-bowel-resective surgery) and controls.* ●, *Postoperative patients, oral administration;* ▲, *postoperative patients, subcutaneous administration;* ○, *controls, oral administration;* △, *controls, subcutaneous administration*

administration shows slightly lower, but not statistically significant, plasma chloroquine levels when compared with parenteral administration. Oral administration is therefore a safe and cheap alternative to parenteral administration. Chloroquine tablets are available at all levels of the health care delivery system. A further advantage of the oral administration is the possibility of increasing easily the dosage depending on the body weight of the patient and on the degree of the prevailing chloroquine sensitivity.

There are very few reports about postoperative incidence of malaria and its treatment[1,2,7–14]. Further studies are required, especially regarding the increase of chloroquine resistance and the introduction of new anti-malarial drugs. In this respect, attention should be paid to Mefloquine, which has, like chloroquine, a very fast resorption, a long half life and does not yet exist in a parenteral form[15–17]. Our study further indicates that it may be cost-effective and efficient to give drugs that are well absorbed in the upper gastrointestinal tract, orally even after abdominal non-bowel-resective surgery.

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References

1. Kark W. Surgery and the relapse rate of malaria. *Br Med J* 1946; **ii**: 114–17.
2. Ajao OG. Malaria and postoperative fever. *J Trop Med Hyg* 1978; **81**: 153–5.
3. Trigg PI, Wernsdorfer WH, Sheth UK, Onori E. Intramuscular chloroquine in children. *Lancet* 1984; **ii**: 288.
4. Clyde DF. *Malaria in Tanzania*. Oxford University Press: London, 1967.
5. Betschard B, Steiger S. Quantitative determination of chloroquine and disethylchloroquine in biological fluids by high performance thin layer chromatography. *Acta Tropica* 1986; **43**: 125–30.
6. Bruce-Chwatt LJ, Black RH, Canfield CJ, Clyde DF, Peters W, Wernsdorfer WH. *Chemotherapy of Malaria*, Monograph Series 27., 2nd ed. Geneva, World Health Organisation 1981.
7. Barrett-Connor E. Postoperative malaria. *Lancet* 1972; **i**: 597–8.
8. Bruce-Chwatt LJ. Postoperative malaria. *Lancet* 1972; **i**: 142.
9. Bruce-Chwatt LJ. Postoperative malaria. *Lancet* 1972; **i**: 1238.
10. Francke EL, Neu HC. Postsplenectomy infection. *Surg Clin North Am* 1981; **61**: 135–55.
11. Maharaj P, McDonald GA, Dobbie JW. Splenectomy and blackwater fever. *Br J Haematol* 1982; **51**: 663–4.
12. Marsepoil T, Blin F, Starkman M, Quinault AM, Sebbah JL, Pellerin M. Accès pernicieux palustre postopératoire chez un sujet originaire d'une zone d'endemie. *Ann Fr Anesth Réanim* 1984; **3**: 371–3.
13. Simpson TW. Postoperative malaria. *Lancet* 1971; **ii**: 1431.
14. Eykyn SJ, Baimbridge MV. Open heart surgery complicated by postoperative malaria. *Lancet* 1977; **ii**: 411–12.
15. Mimica I, Fry W, Eckert G, Schwarzt DE. Multiple-dose kinetic study of Mefloquine in healthy male volunteers. *Chemotherapy* 1983; **29**: 184–7.
16. Schwartz DE, Eckert G, Hartman D *et al.* Single-Dose kinetics of Mefloquine in man. *Chemotherapy* 1982; **28**: 70–84.
17. Chanthavanich P, Looareesuwan S, White NJ *et al.* Intragastric mefloquine is absorbed rapidly in patients with cerebral malaria. *Am J Trop Med Hyg* 1985; **34**: 1028–36.

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Kinetics of intra-operative pH of the canine corpus fundal mucosa before and after truncal vagotomy

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The intra-operative surface pH of the corpus fundic mucosa in anaesthetized dogs was studied with a glass electrode during stimulation with graded doses of pentagastrin. The mucosal pH could be related to the dose of pentagastrin by a hyperbolic curve. With intact vagus ED$_{50}$ *averaged 0·67 μg kg* $^{-1}$ *h*$^{-1}$ *of pentagastrin and maximum effect corresponded to an average pH of 1·9. Immediately after truncal vagotomy there was a significant shift of the curve to the right corresponding to an average* ED$_{50}$ *of 3·77 μg kg*$^{-1}$ *h*$^{-1}$*, an effect that could be described as that of a competitive inhibitor. Two weeks after vagotomy the value of* ED$_{50}$ *had returned to the prevagotomy level. The high* ED$_{50}$ *immediately after vagotomy is ascribed to the sudden fall in the subthreshold release of acetylcholine previously supplied by the intact vagus. The return to the low* ED$_{50}$ *2 weeks later could be explained by denervation supersensitivity. The relation between the curves before and immediately after vagotomy suggests that the dose of the agonist be as low as possible, when testing the completeness of a vagotomy intra-operatively.*

Keywords: Dose–response curves, gastric mucosal pH, pentagastrin, vagotomy

Intra-operative measurements before and after vagotomy of the surface pH on human[1,2] and canine[3] corpus fundic mucosa have revealed a rise in pH to 4·0–7·0 immediately after vagotomy during stimulation with histamine[1], ametazole[2] or pentagastrin[2–4]. Intact vagal branches result in corresponding areas of intact low pH and hence intra-operative pH measurements can be used to assess the completeness of a vagotomy. The procedure is known as the Grassi test[5].

The pH change immediately after vagotomy can be explained by experiments showing a transient period of profound reduction of the responsiveness of the parietal cells of very short duration (24 h) in man[6] and the dog[3].

The purpose of the present investigation was to characterize further the mechanism responsible for the above changes by studying the effect of graded doses of pentagastrin on the intra-operative pH of the canine corpus fundic mucosa before and after vagotomy.

Methods

Twenty-one mongrel dogs weighing 13–26 kg were used. Before each experiment, food but not water was withheld for 18 h.

Surgical procedures

Pentobarbital sodium (usually 30 mg kg^{-1}) was used for induction of anaesthesia to a level at which the reflex of eyelid contraction in response to stroking the periorbital skin was suppressed. Artificial respiration at a rate of 0·25 litres kg^{-1} of nitrous oxide and oxygen in a ratio of 4:1 was routinely used.

At the first operation, when pH measurements before vagotomy were made, a gastrotomy (longitudinal and 3–4 cm long) was made in the distal and anterior part of the corpus to provide an entrance for the pH electrode. After the measurements had been made, the gastrotomy was closed around a gastric cannula (inner diameter 2 cm), which was brought to the surface through a stab wound in the abdominal wall. This cannula was only used for secretion tests on conscious dogs and was dissected from the abdominal wall and the stomach at later operations to recreate the gastrotomy through which the electrode was introduced. At the second operation, pH measurements were made following transthoracic truncal vagotomy. At the third operation, only pH measurements were made.

pH measurements

For every pH measurement laparotomy was performed during anaesthesia[3,7]. A calomel electrode (K 401, Radiometer, Denmark) was placed in contact with the animal's tongue. A glass electrode (G 202 C, Radiometer) was introduced through the above mentioned entrance in the gastric wall. The tip of the glass electrode was placed in contact with the mucosa with gentle pressure and the mucosa was traversed by the electrode from the fundus to the pylorus in three approximately parallel columns to record gastric mucosal pH at 1–2 cm intervals (*Figure 1*).

Pentagastrin (Peptavlon®, ICI) in the doses 0·5–6·0 μg kg^{-1} h^{-1} was added to an intravenous infusion of saline (50 ml h^{-1}) and was given for at least 20 min before measurements were made. In dose–response experiments, the doses were 2·0, 6·0 and 12·0 μg kg^{-1} h^{-1} immediately after vagotomy; before vagotomy and at 2 weeks afterwards measurements were made during basal conditions and at doses of 0·5 and 2·0 μg kg^{-1} h^{-1}.

Before each pH measurement the mucosa was carefully cleaned by instillation of saline and gentle suction with a plastic surgical suction tube (type 0100, AB Medena, Kungsbacka, Sweden) and by using gauze swabs. After cleaning, 6 min were allowed to pass before measurements were made. At the dose of 0·5 μg kg^{-1} h^{-1} the procedure differed slightly; as these recordings were made after basal measurements when pH was high, no additional cleaning was considered necessary. These measurements were made after an average infusion time of 16 min for reasons explained elsewhere[7].

Insulin tests

These experiments were made on conscious dogs as described elsewhere[3].

Statistics

The pH values of the antrum were excluded from the calculations[7]. The pH recording at each dose level then comprised about 50 measurement spots (*Figure 1*). Since pH values have a normal distribution around the mean[8], an average was calculated directly from these logarithmic values to represent the result of the individual dog on that occasion.

The results were analysed by a computer program based on a method of least squares described by Parker and Waud[9]. The assumption that the agonist acts reversibly with the receptor, conforming to the law of mass action, predicts a sigmoid curve when the logarithm of the dose is plotted on the abscissa. This can be modelled by a rectangular hyperbolic relationship between the dose of the agonist

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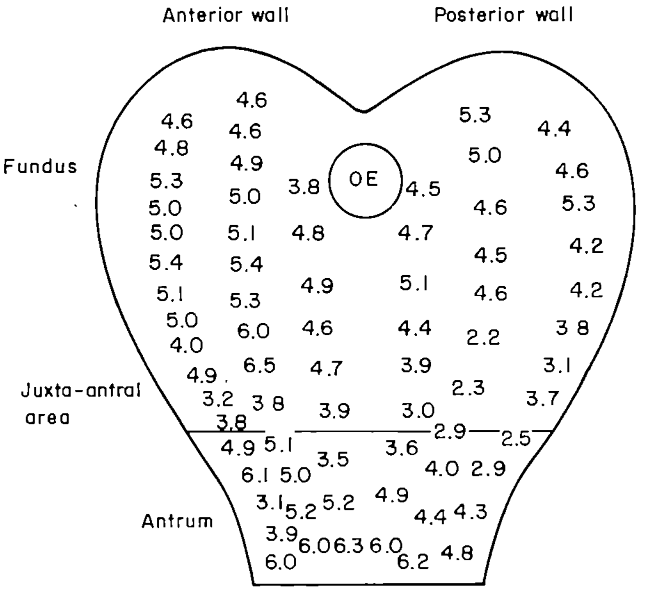

Figure 1 *Diagram of the mucosal surface of a stomach opened along the greater curvature. The pH values indicated represent a recording immediately after truncal vagotomy during stimulation with 2·0 µg kg^{-1} h^{-1} of pentagastrin. When the values of the antrum were excluded, mean pH was 4·5 and the median was 4·6 (range 2·2–6·5) implying a normal distribution; the former value was used for the construction of the dose–response curves*

and the response. The equation is thus

$$E_{\text{obs}}=\frac{M\times A^{p}}{A^{p}+ED_{50}{}^{p}}$$

where E_{obs} is the observed response to the dose A. The three unknown variables to be calculated are: M, the maximum response; ED_{50}, the dose of pentagastrin producing one half M and p, the slope of the logistic function. Since the function increases with the dose, it was necessary to feed the computer with the difference between pH 7·0 and the observed pH values.

From the pooled values, conclusions could be made that led to a reasonable approximation of maximum effect i.e. the minimum of the mucosal pH. The responses at 2·0 and 6·0 µg kg^{-1} h^{-1} were almost at the same level, indicating that the curve had levelled out. Since the calculated maximum effect exceeded the response obtained at 2·0 µg by 5·5 per cent it seemed reasonable to fix M in the program at a value 5·5 per cent higher, i.e. pH-wise 5·5 per cent lower, than the response observed at 2·0 µg. The utilization of a 5·5 per cent higher effect as maximum obviated a serious overestimation of the value of p.

According to the equation, the response is zero at the dose zero, and hence the basal response should be subtracted from the observed values[10–14]. However, this was not done in the present investigation since no basal recordings were performed immediately after vagotomy.

Results

The data from all the dogs investigated before vagotomy were pooled and the mean mucosal pH values obtained at the various dose levels were related to the dose of pentagastrin by the logistic function according to the computer program. The correlation coefficient for this adjustment was 0·94. Maximum calculated effect corresponded to a pH value of 1·9; ED_{50} was 0·67 µg kg^{-1}h^{-1} of pentagastrin and the value of p was 2·0. The hyperbolic curve for the pooled values of the mucosal pH is shown in *Figure 2*.

When the pooled values obtained at 2·0 µg kg^{-1} h^{-1} (mean pH = 2·2, $n=14$) were compared with the values registered at 6·0 µg kg^{-1} h^{-1} (mean pH = 2·0, $n=7$), there was no significant difference ($P>0{\cdot}5$, unpaired t test).

Mucosal pH was related to the dose of pentagastrin by the logistic function in the individual dog with M fixed at a value that exceeded the effect observed at 2·0 µg kg^{-1} h^{-1} by 5·5 per cent. The median value of the correlation coefficients was 0·98 (range 0·69–1·00). Maximum effect corresponded to a pH of 1·9 ± 0·3 (mean ± 95 per cent confidence limits, $n=13$). ED_{50} was 0·67 ± 0·11 µg kg^{-1} h^{-1} of pentagastrin. The value of p was 2·8 ± 0·5.

In order to investigate whether the response obtained at 0·5 µg represented a reasonable estimate of a steady state, the measurements at this dose were repeated after the duration of the infusion time had been prolonged 2–3 times, still without previous cleaning. By substituting the response obtained after the shorter duration of the infusion at 0·5 µg kg^{-1} h^{-1}, the effect on the curves was evaluated. Thus, an original ED_{50} of 0·61 ± 0·18 µg kg^{-1} h^{-1} (mean ± 95 per cent confidence limits, $n=4$) was obtained after an average of 16 min infusion of 0·5 µg. A prolongation of the infusion time of this dose to an average of 41 min resulted in a calculation of an ED_{50} value of 0·45 ± 0·15 µg kg^{-1} h^{-1}. The difference between these ED_{50} values was not significant ($P>0{\cdot}05$, paired t test).

Four dogs were investigated with graded doses of pentagastrin both before and immediately after vagotomy. The median value of the correlation coefficients was 0·98 (range 0·69–0·99) before and 0·97 (range 0·81–1·00) immediately after vagotomy. Maximum effect corresponded to a pH value of 1·7 ± 0·4 (mean ± 95 per cent confidence limits) before and 2·3 ± 0·9 immediately after vagotomy. The difference in M was not significant ($P>0{\cdot}1$, paired t test). ED_{50} was 0·79 ± 0·32 µg kg^{-1} h^{-1} of pentagastrin before and 3·77 ± 1·78 µg kg^{-1} h^{-1} immediately after vagotomy. The difference between the ED_{50} values was significant ($P<0{\cdot}02$). The value of p was 3·3 ± 1·6 before and 1·8 ± 0·7 immediately after vagotomy, a change that was not significant ($P>0{\cdot}1$). The hyperbolic curves for the mucosal pH before and immediately after vagotomy are shown in *Figure 3*.

Three dogs were investigated two weeks after vagotomy. The median value of the correlation coefficients was 0·96 (range 0·45–0·98). Maximum effect corresponded to a pH of 2·1 ± 1·7 (mean ± 95 per cent confidence limits). ED_{50} was 0·65 ± 0·22 µg kg^{-1} h^{-1} of pentagastrin. The value of p was 2·6 ± 0·8.

Average values of the two highest consecutive 15 min periods of acid output after the intravenous injection of insulin (0·02 units kg^{-1}) to conscious dogs were 444·4 ± 340·7 µmol min^{-1} (mean ± 95 per cent confidence limits, $n=6$) before vagotomy and 4·5 ± 2·5 µmol min^{-1} after vagotomy. All postvagotomy tests were negative according to Hollander's criteria.

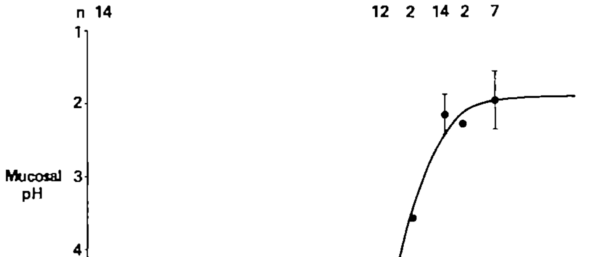

Figure 2 *Pentagastrin dose–response curve fitted by computer for the intra-operative pH of the corpus fundic mucosa. The points represent the mean ± 95 per cent confidence limits of the observed values. The number of dogs* (n) *investigated at each dose level is indicated at the top*

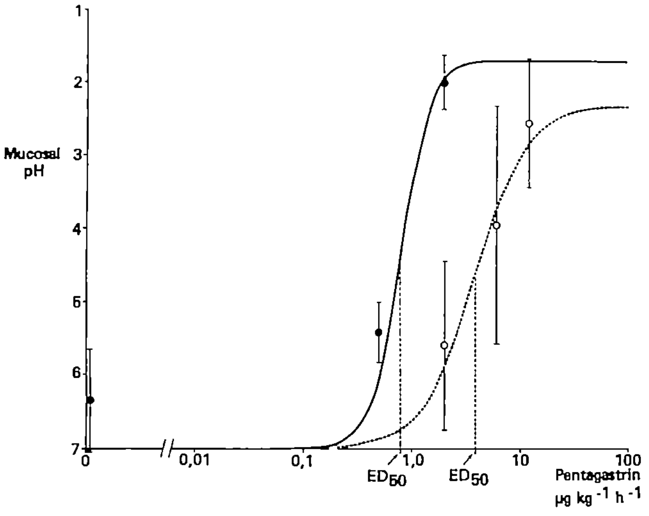

Figure 3 *Pentagastrin dose–response curves fitted by computer for the intra-operative pH of the corpus fundic mucosa before*, ●, *and immediately after*, ○, *truncal vagotomy. Both curves represent the mean values of* M, ED_{50} *and* p *obtained from the individual curves of four dogs. The points represent the mean* ± *95 per cent confidence limits of the observed values*

Discussion

The present investigation shows that the response of the intra-operative pH of the corpus fundic mucosa to pentagastrin could be described by the rectangular hyperbola with the same high correlation as in previous experiments involving acid secretion and mucosal blood flow in the dog$^{10-13}$ and man^{14}. The fixing of maximum effect in the individual dog to a value that exceeded the response observed at 2·0 µg kg^{-1} h^{-1} by 5·5 per cent resulted in an average ED_{50} identical with that of the pooled values, a circumstance that confirms the feasibility of an earlier recommendation to fix maximum effect at a reasonable value^{15}.

The mucosal pH corresponded to that layer of gastric juice covering the mucosal surface after 6 min of secretion. An exception was made for the dose of 0·5 µg kg^{-1} h^{-1} of pentagastrin, in that measurements were made after an average infusion time of 16 min. Since the preceeding basal measurements were almost anacid, it seemed unnecessary to do additional cleaning before the recordings at that dose. Although the plasma concentration of pentagastrin levels out 10 min after the onset of infusion^{7}, the acid secretion might not reach the mucosal surface until later and the effective time for build-up of mucosal pH might have been reduced in comparison with the other dosages. However, when the duration of infusion was raised to an average of 41 min, the influence on the value of ED_{50} was not significant. The above irregularity in technique could therefore be considered as unimportant.

Immediately after vagotomy, there was an approximately parallel shift of the dose response curve to the right, corresponding to a five-fold increase in ED_{50}, indicating a highly decreased sensitivity of the parietal cell mass. This shift to the right must be considered a specific effect of the vagotomy, since control experiments in man^{2} and in the dog^{3} have shown that a prolongation of the duration of the anaesthesia is without effect on the intra-operative pH. The change in maximum effect was not significant, but it should be noted that the rise in pH immediately after vagotomy averaged 30 per cent and some influence on maximum effect could not be completely excluded by the present investigation. It is possible, however, that this difference would have disappeared, had the curves been followed till they levelled out. Since a significant increase in ED_{50} was the main effect, the immediate influence of vagotomy on intra-operative mucosal pH could be described as one of competitive inhibition.

During basal conditions before vagotomy, an average pH of 6·0 was noted (*Figure 2*). This may be considered the result of a threshold-subthreshold activity of the vagus. Such subthreshold activity of the vagus can potentiate the response to pentagastrin^{16}. The shift of the dose–response curve to the right immediately after vagotomy is therefore well explained by a reduction of the threshold–subthreshold release of acetylcholine previously supplied by the intact vagus. Two weeks after vagotomy, ED_{50} had returned to the prevagotomy level. Since it has been shown that the period of profound reduction of the responsiveness of the parietal cells is over within 24 h of vagotomy^{3,6}, it must be assumed that ED_{50} returns to a low level within that interval. Experiments on dogs with denervated gastric pouches implies a subthreshold release of acetylcholine from autonomously working postganglionic fibres^{17}. Denervation supersensitivity to cholinomimetic stimulus has been noted when gastric pouches were denervated^{18}, and in the gastric fistula dog after vagotomy^{3}. Such supersensitivity could therefore restore vagal tonus, and hence explain the return to the low ED_{50} within 2 weeks of vagotomy.

A 35 per cent decrease in basal mucosal blood flow immediately after truncal vagotomy and a return to prevagotomy values 3 weeks later have been found in the dog^{19} and a similar reaction can be compiled from other studies^{20,21}. It is known that the curve for blood flow lies a considerable distance to the left of that for acid output in response to histamine and pentagastrin^{11} so that the ratio blood flow/acid output is high at the beginning of the dose–response curve and gradually decreases as maximum acid output is approached. A 35 per cent reduction in blood flow is therefore not likely to influence the ED_{50} for acid output or explain a five-fold increase in ED_{50} for intra-operative pH. An influence on maximum effect would be expected and would explain the moderate rise in pH immediately after vagotomy, although this was not significant. Since the microvasculature is more sensitive to cholinergic stimulation that is the parietal cell^{13}, it must be considered that both the reduction in blood flow and the highly decreased sensitivity of the parietal cell mass immediately after vagotomy depend on the decrease in the threshold–subthreshold release of acetylcholine.

It is obvious from *Figure 3* that infusion of a continuous dose of 12 µg kg^{-1} h^{-1} of pentagastrin results in a small change in pH after vagotomy, whereas a dose of 2 µg kg^{-1} h^{-1} effects a sharp drop in pH in the immediate postvagotomy period. Therefore, a low dose should be employed, to assess the completeness of vagotomy by the Grassi test.

Because the distal, juxtra-antral area is the most sensitive part of the parietal cell mass in response to pentagastrin^{7,11} and because of the variable relation between the antrofundic border and the insertion of the antral nerve in the lesser curvature in man^{2,22,23} there are good reasons to employ the Grassi test when performing highly selective vagotomy. This allows evaluation of how much of the antral nerve should be sectioned in the juxtra-antral part of its course. However, acid spots in the juxtra-antral part of the parietal cell mass may result as a consequence of this area's greater sensitivity to pentagastrin as seen in the experiment depicted in *Figure 1*, when spots of pH < 4·0 were noted in this area in spite of an insulin negative truncal vagotomy. Since in response to histamine the distal part of the parietal cell mass is the least sensitive area^{12}, acid spots in the juxtra-antral area after highly selective vagotomy can only depend on remaining vagal innervation when this agonist is used. Histamine or histamine analogues therefore seem to be the suitable agonists for intra-operative stimulation. It should be noted that histamine was the agonist originally used by Grassi for this purpose^{1,5,22}.

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References

1. Grassi G. A new test for complete nerve section during vagotomy. *Br J Surg* 1971; **58**: 187–9.
2. Larsson JO. Studies of the pH value of the gastric mucosa before and after vagotomy. *Gazetta Sanitaria* 1973; **22**: 91–8.
3. Larsson JO. Intraoperative pH of the gastric mucosa before and after truncal vagotomy in the dog. *Scand J Gastroenterol* 1984; **19**: 65–70.
4. Johnson AG, Baxter HK. Where is your vagotomy complete? Observations on operative technique. *Br J Surg* 1977; **64**: 583–6.
5. Grassi G, Orecchia C, Cantarelli I, Fivoli E, Sbuelz B. Risultati e considerazioni sullo studio della secrezione gastrica nella malattia ulcerosa in fase operatoria. *Chir Gastroent* 1969; **3**: 465–74.
6. Larsson JO. Demonstration of a refractory period of the parietal cell after vagotomy with special reference to the Grassi test. *Chir Gastroent* 1973; **7**: 367–77.
7. Larsson JO. Regional differences in the kinetics of the canine parietal cell mass in response to pentagastrin. *Surg Gynecol Obstet* 1981; **153**: 169–76.
8. Mitchell RD, Hunt JN, Grossman MI. Inhibition of basal and postprandial gastric secretion by poldine and atropine in patients with peptic ulcer. *Gastroenterology* 1962; **43**: 400–6.
9. Parker RB, Waud DR. Pharmacological estimation of drug-receptor dissociation constants. Statistical evaluation. I. Agonists. *J Pharmacol Exp Ther* 1971; **177**: 1–12.
10. Knight SE, McIsaac RL, Rennie CD. Sensitivity of the parietal cell and microvasculature to histamine antagonists in the dog. *Br J Pharmacol* 1979; **66**: 458P.
11. Larsson JO. Difference in kinetics between the distal and proximal parts of the canine parietal cell mass in response to pentagastrin. *J Physiol* 1982; **327**: 507–17.
12. Larsson JO. Difference in kinetics between the distal and proximal parts of the canine parietal cell mass in response to histamine. *J Physiol* 1983; **335**: 113–21.
13. Larsson JO. Acid secretion and mucosal blood flow in the distal and proximal parts of the canine parietal cell mass in response to cholinergic stimulation. *Scand J Gastroenterol* 1985; **20**: 1209–16.
14. Knight SE, McIsaac RL, Rennie CD. The effect of histamine and histamine antagonists on gastric acid secretion and mucosal blood flow in man. *Br J Surg* 1980; **67**: 266–8.
15. Waud DR, Parker RB. Pharmacological estimation of drug-receptor dissociation constants. Statistical evaluation II. Competitive antagonists. *J Pharmacol Exp Ther* 1971; **177**: 13–24.
16. Sjödin L. Gastric acid responses to graded vagal stimulation in the anaesthetized cat. *Digestion* 1975; **12**: 17–24.
17. Code CF, Hightower NC, Hallenbeck GA. Comparison of the effects of methanteline bromide (Banthine) and atropine on the secretory responses of vagally innervated and vagally denervated gastric pouches. *Gastroenterology* 1951; **19**: 254–64.
18. Brooks AM, Stening GF, Grossman MI. Effect of gastric vagal denervation on inhibition of acid secretion by secretin. *Am J Dig Dis* 1971; **16**: 193–202.
19. Lenz J, Seifert J, Brendel W, Holle F. Messung der Magenwanddurchblutung beim Hund mit radioactiven Microspheres nach trunculärer Vagotomie. *Chir Forum Exp Klin Forsch* 1977: 199–202.
20. Bell PRF, Battersby C. Effect of vagotomy on gastric mucosal blood flow. *Gastroenterology* 1968; **54**: 1032–7.
21. McIsaac RL, Johnston BJ, Fielding LP, Dudley HAF. Basal and dose-response studies of gastric mucosal blood flow: Comparison of duodenal ulcer patients before and after highly selective vagotomy with normal volunteers. *World J Surg* 1982; **6**: 427–32.
22. Hedenstedt S, Grassi G. The completeness of selective proximal vagotomy tested peroperatively with pH-metry. *Acta Chir Scand* 1971; **137**: 551–4.
23. Poppen B, Delin A, Sandstedt B. Parietal cell vagotomy. Localisation of the microscopical antral-fundic boundary in relation to the macroscopical. *Acta Chir Scand* 1976; **142**: 251–5.

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Management of caustic ingestion in adults

The treatment of 484 adults with caustic ingestion injury is discussed. Signs and symptoms are an unreliable guide to injury and a chest X-ray and fibreoptic endoscopy should be performed as soon as possible. All of the 250 patients who developed superficial lesions of the oesophagus, stomach or duodenum experienced healing without sequelae. Forty-four patients required emergency surgery of whom twenty-four died and oesophagectomy without thoracotomy is now advocated for this group, followed by interval surgery to restore continuity. The remaining 190 patients suffered gastric or oesophageal ulceration without necrosis: 92 recovered without complication, 3 succumbed to aorto-oesophageal fistula, 12 survived following delayed surgery for complications and 83 developed oesophageal and/or gastric stenosis which subsequently required endoscopic or surgical treatment.

Keywords: Caustic ingestion, oesophagectomy

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The high frequency of caustic ingestion in France is due to the unrestricted sale of corrosive products, usually without sufficient instructions for use. In this review of the records of the Paris Anti-Poison Center over the 13 years up to 1 October 1983 we will consider 484 patients who were admitted with caustic ingestion burns. Guidelines for management are presented.

Patients and methods

Between 1 January 1971 and 1 October 1983, 484 patients were admitted to our department after caustic ingestion caused either by accident (38 cases) or by suicide attempts. The Anti-Poison Center of Paris comprises an intensive care unit, a surgery department and a digestive and respiratory endoscopy department. Most of the 263 females and 221 males treated were adults; 416 of the patients ranged in age from 18 to 50 years. The types of caustic products ingested are shown in *Table 1*.

On admission all patients underwent a thorough clinical examination, a chest X-ray to eliminate any mediastinal complication or bronchial inhalation, and an oesophagogastroduodenal endoscopy examination. Management was determined by the seriousness of the first clinical survey and, above all, by the results of endoscopy. Endoscopic lesions were classified as: stage I, mucosal hyperaemia without ulceration; stage II, ulcerations which appeared to have spread beyond the submucosa; and stage III, no remaining sound mucosa, necrosis or deep ulcers.

Kissing ulcers of the oesophagus or circumferential ulcerations which would lead to stenosis were classified as stage IIb lesions. All the patients with mucosal ulcerations or necrosis had antibiotic cover by penicillin G and metronidazole.

Patients were classified in three groups as follows.

Group 1: patients showing superficial caustic burns of the stomach and or the oesophagus defined as hyperaemia without ulceration.

Group 2: patients requiring emergency surgery. These were patients with a history of massive ingestion of strong acid or base (more than one glass full of liquid or approximately 150 ml). The fibreoptic examination showed in every case an extensive black necrosis of all the oesophageal and gastric mucosa and an atonic gut. These patients presented with signs of shock with agitation, tachypnoea and cardiovascular collapse, and all showed marked acidosis.

Group 3: patients who did not need emergency surgery but in whom endoscopy showed gastric and oesophageal ulceration with false membranes but no necrosis.

Results

All of the 250 group 1 patients who presented with superficial lesions healed without any sequelae.

Table 1 *Caustic products ingested in 484 patients*

Caustic products	Number of patients
Sodium hydroxide	164
Chlorine bleach	193
Hydrochloric acid	88
Sulphuric acid	28
Ammonia	9
Oxalic acid	1
Nitric acid	1
Total	484

Table 2 *Outcome in 44 patients undergoing emergency surgery following caustic ingestion*

Surgical procedures	Number of patients	Mortality
Laparotomy (acute caustic peritonitis)	10	10
Oesophagogastrectomy with thoracotomy	11	7
Oesophagogastrectomy without thoracotomy	23	7

Of the 44 group 2 patients undergoing emergency surgery, 24 died (*Table 2*). Ten patients died after a heavy intake which led to caustic peritonitis following gastric perforation. Eleven patients underwent oesophagogastrectomy with thoracotomy and seven died, but the procedure of oesophagectomy without thoracotomy introduced in 1979 was safer in that of the 23 patients undergoing this operation only 7 died. The 20 patients who survived oesophagectomy underwent subsequent oesophagoplasty (13 cases) or oesophagopharyngoplasty (7 cases) without mortality.

Of the 190 patients in the third group, 3 died between the fifteenth and thirtieth day because of an aorto-oesophageal fistula. Ninety-two patients recovered without sequelae. Eighty-three patients developed gastric and/or oesophageal stenosis (*Table 3*) which required endoscopic or surgical treatment. Two of them died because of complications of oesophagoplasty (graft necrosis), nineteen had developed an antral stricture which was treated successfully by partial gastrectomy and seven patients developed a mild oesophageal stricture which was efficiently treated by endoscopic dilatation. A further 12 group 3 patients required delayed surgery because of the development of complications (*Table 4*).

In all, 70 patients underwent oesophageal reconstruction by ileocoloplasty, in 50 cases for a non-dilatable oesophageal stricture and in 20 following emergency oesophagogastrectomy. Seven patients required oesophagopharyngoplasty.

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Table 3 *Treatment of the gastric and oesophageal sequelae of caustic ingestion in 83 patients*

Sequela	Number of patients	Treatment	Mortality
Antral stricture	19	Hemigastrectomy	0
Short oesophageal stricture	7	Instrumental dilatation	0
Long tight oesophageal stricture	50	Oesophagoplasty (ileocoloplasty)	2
Severe oesophagopharyngeal stricture	7	Oesophagopharyngoplasty (ileocoloplasty)	0

Table 4 *Acute complications following caustic ingestion in 12 patients*

Complication	Number of patients	Treatment	Mortality
Gastric haemorrhage	3	Gastrectomy 2 Haemostasis 1	—
Occluded gastric perforation	5	Hemigastrectomy	—
Gastrocolic fistula	2	Hemigastrectomy and colectomy	—
Secondary oesophagotracheal fistula	2	Fistula exclusion	—

Table 5 *Causes of death following caustic ingestion*

Time of death	Cause	Number of patients
Late	Complications of oesophagoplasty	2
Secondary	Aorto-oesophageal fistula	3
Early	Caustic peritonitis	10
	Complications of oesophagogastrectomy	
	Tracheal and bronchial necrosis	9
	Acute pancreatitis	1
	Gas gangrene	1
	Septicaemia	1
	Disseminated intravascular coagulation	1
	Mediastinal haemorrhage	1
Total		29

Of the 64 patients who survived oesophagoplasty, 2 died, 45 had good immediate results while 17 needed one or several endoscopic dilatations of a stricture at the cervical anastomosis. Among the seven patients with oesophagopharyngoplasty, five ate normally after a few months of re-education, one needed repeated endoscopic dilatations, and one was a failure of treatment in that tube feeding by jejunostomy is now required.

The overall mortality of this series of patients is shown in *Table 5*.

Discussion

Patients who have ingested caustic solutions can be adequately treated in a hospital equipped with an intensive care unit and a unit where both upper digestive tract and respiratory tract endoscopy are performed. Associated drug intake connected with suicide attempts have to be dealt with in collaboration with an Anti-Poison Center. Upon admission, it is vital to establish the nature and the amount of the corrosive agent ingested, the depth and the extent of the lesions, and the need for emergency medical or surgical treatment.

The initial clinical examinations may be enough to ascertain the need for urgent surgery because of peritonism with pneumoperitoneum or cervical subcutaneous emphysema due to oesophageal perforation. Despite urgent surgery the prognosis in these cases is gloomy and massive caustic peritonitis is usually fatal. This was the case in 10 of our patients, all of whom had a history of massive ingestion of concentrated acid or base and most importantly a long time (>12 h) between ingestion and surgery.

The patient's signs and symptoms do not usually give a reliable forecast of oesophageal injury[1]. In the first few hours the clinical picture is often frightening with agonizing buccal, retrosternal and epigastric pain accompanied by dysphagia and nausea. Endoscopy is essential to define the severity and extent of injury. Daly[2] and Yarrington *et al.*[3] found oesophageal lesions in 15 to 23 per cent of cases who had no obvious oropharyngeal damage. The fibreoptic examination has to be performed as soon as possible, preferably within the first 24 h and most authors now advocate a thorough examination of the oesophagus and the stomach[4]. The risks of this full examination are small; Di Costanzo[4] recorded no complication in 127 examinations of 35 patients and we have experienced no problems during the first endoscopic examination, even though in two cases endoscopy was performed 48 h after caustic ingestion. Lesions of different stages are often concomitant, and it may be very difficult to evaluate the depth of burns if there is covering false membrane. In our opinion, the surgeon must be present at endoscopy to evaluate the need for surgical treatment.

Patients with stage I lesions should be given parenteral nutrition in the expectation that the lesions will heal in every case. We do not use antidotes because healing in stage I lesions is spontaneous, while antidotes are inefficient in patients with severe damage[4].

Some patients show extensive lesions with necrosis of the oesophagus and the stomach at endoscopy. There is often massive early acidosis and coagulation disorders with fibrinolysis. We believe that immediate surgery is needed in such patients to avoid massive perforation of the trachea[5]. This indication for immediate surgery has been proposed by others[6–8]. The operation usually consists of total gastrectomy and transhiatal oesophagectomy without thoracotomy[9], and this emergency approach has proved effective in patients who have ingested large amounts of strong acid or alkali. In these patients with very deep and extensive burns of the oesophagus, tracheal and bronchial injury may occur in the course of ingestion or vomiting; the respiratory tract may be intact initially but becomes involved gradually by extension of the mediastinal necrosis[5,7]. Of our ten patients who presented with tracheobronchial necrosis, nine died and only one survived after surgical intervention 10 days later, during which the back wall of the trachea was patched with the right upper lobe of the lung. Eight of these ten patients were operated on >12 h after ingestion and we consider that early excision of the oesophagus is imperative if extension of the necrosis is to be restricted. Patients with severe caustic burns (stages II, IIb and III) should be given parenteral nutrition[4]. During the third week a second fibreoptic endoscopy and an oesophagogram with water soluble contrast are advised. After administering corticosteroids[10] to such patients we found like Oakes[11] that this did not prevent the development of stenosis. The inefficiency of cortisone in preventing stenosis has been experimentally demonstrated by Knox[12].

During the first two weeks, complications such as gastric haemorrhage and perforation, or gastrocolic fistula can still occur. Three of our patients died of an aorto-oesophageal fistula after two weeks. Secondary tracheo-oesophageal fistulae heal readily after cervical oesophagostomy (as in two of our patients) and more complex procedures[13] do not seem necessary.

The timing of non-urgent surgery is dictated by the location of the lesions. In our experience the lesions become cicatrical on the stomach earlier than the oesophagus. If only the stomach is affected an operation can be performed after the second month; if the oesophagus is involved it is usually postponed until the end of the third month when all the lesions are cicatrized. Different situations may arise. In the case of antral stricture with a normal oesophagus, partial gastrectomy or gastrojejunostomy suffices; we prefer partial gastrectomy because of the risks of secondary stenosis and anastomotic ulcer following gastro-enterostomy. In the case of oesophageal stricture, lesions which have a lumen > 10 mm in diameter do not often impede normal life and should be left alone. Some patients have a short stricture with significant narrowing of the lumen of the oesophagus, and instrumental dilatation gives good results[14]. A severe and long narrowing of the oesophagus makes oesophagoplasty mandatory. We never use instrumental dilatation in such stenosis as it is dangerous and has to be repeated many times; indeed this multiple trauma has been implicated in malignant degeneration[15]. It is still possible to perform a total oesophagoplasty even if the lesions involve the pharynx[16].

Some authors[17,18] insist that the burned oesophagus should be removed, but we think that the oesophagectomy is not always necessary. Removal of the scarred oesophagus is extremely difficult and dangerous, and the risk of complication due to retaining the oesophagus seems very limited. Mucocysts are rare and develop only if continuity with the stomach is missing. The risk of cancer is very difficult to assess[19-21] but there is scant evidence that the burn plays a part in the development of such cancers considering that the reported delays were 41 or 45 years[15,19]. None of our patients has developed cancer of the remaining oesophagus but our long term follow up is at present only 13 years.

References

1. Gaudreault P, Parent M, McGuigan MM, Chicoine L. Predictability of esophageal injury from signs and symptoms. A study of caustic ingestion in 378 children. *Pediatrics* 1983; **71**: 767–70.
2. Daly JF. Acute corrosive esophagus. *Arch Otol* 1961; **24**: 629.
3. Yarrington CT, Bales GA, Frazer JP. A study of management of caustic esophageal trauma. *Ann Otol Laryngol* 1964; **37**: 130.
4. Di Costanzo J, Noirclerc M, Jouglard J, Escoffier JM, Cano M, Martin J, Gauthier A. New therapeutic approach to corrosive burns of the upper gastrointestinal tract. *J Br Soc Gastroenterology* 1980; **21**: 370–5.
5. Deneuville M, Andreassian B, Charbonnier JY, Assens P, Dubost CL, Celerier M. Complications trachéo-bronchiques graves des ingestions de caustiques chez l'adulte. *J Chir (Paris)* 1984; **121**: 1–6.
6. Gago O, Ritter FN, Martel W *et al.* Aggressive surgical treatment for caustic injury of the esophagus and stomach. *Ann Thoracic Surg* 1972; **13**: 243–9.
7. Kirsch MM, Peterson A, Brown JW, Orringer MB, Ritter FN, Sloan H. Treatment of caustic injuries of the esophagus: a ten years experience. *Ann Surg* 1978; **188**: 675–8.
8. Nancy P, Manach Y. Traitment d'urgence d'une brolure récents de l'oesophage. *Ann Otol Laryngol* 1978; **6**: 361–6.
9. Brun JG, Celerier M, Koskas F, Dubost CI. Blunt thorax oesophageal stripping: an emergency procedure for caustic ingestion. *Br J Surg* 1984; **71**: 698–700.
10. Symbas PN, Vlasis SE, Hatcher CR. Esophagitis secondary to ingestion of caustic material. *Am Thorac Surg* 1983; **36**: 73–7.
11. Oakes DD, Sherck JP, Mark CR. Lye ingestion. Clinical patterns and therapeutic implications. *J Thoracic Cardiovasc Surg* 1982; **83**: 194–204.
12. Knox WG, Scott JR, Luitel HA. Bougierage and stenoids used singly or in combination in experimental corrosives esophagitis. *Ann Surg* 1967; **166**: 930.
13. Burnington JD, Raffensperger JG. Surgical management of tracheo-oesophageal fistula complicating caustic ingestion *Surgery* 1978; **84**: 329–34.
14. Desnos J, Dubin J, Darsonval V. Résultats à long terme de la dilatation par la méthode des sondes-bougies, des sténoses après oesophagite caustique. *Ann Otol Laryngol* 1978; **5**: 401–9.
15. Hopkins RA, Postlethwait RW. Caustic burns and carcinoma of the esophagus. *Ann Surg* 1981; **194**: 146–8.
16. Mislawski R, Brun JG, Ferry J, Tran Ba Huy P, Frachet B, Beutter P. Sténoses digestives caustiques interessant l'hypopharynx. Oesophagopharyngoplastie par greffon iléocolique droit. *Nouv Presse Med* 1982; **11**: 2921–4.
17. Gaillard J, Haguen Auer JP, Romanet P. La dégénérescence cancéreuse des sténoses cicatricielles (par caustiques) de l'oesophage. *Ann Otol Laryngol* 1978; **95**: 395–9.
18. Thomas H, Arthur O. Pharyngoesophageal caustic stricture. Treatment by pharyngogastroplasty compared to colon interposition combined with free bowel graft. *Am J Surg* 1976; **132**: 195–203.
19. Appelquist P, Salmo M. Lye corrosion carcinoma of the esophagus: a review of 633 cases. *Cancer* 1980; **45**: 2655–8.
20. Carven GM Jr, Scaly WC, Dillon ML. Management of alcali burns of the oesophagus. *J Am Med Assoc* 1956; **160**: 1477.
21. Kiviranta UK. Corrosion carcinoma of the esophagus. *Acta Otol Laryngol* 1952; **102**: 1.

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Gangrene of the right colon: a rare complication of trauma-related systemic hypotension

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Hypotensive ischaemia of the colon has been described associated with non-abdominal trauma[1], congestive cardiac failure[2] and pancreatitis[3]. This usually causes merely mucosal damage and only ten cases of gangrenous colon associated with systemic hypotension from non-abdominal trauma have been reported in the English literature.

Case report

A previously healthy 16-year-old boy sustained close-range low velocity gunshot wounds to his penis and right thigh. On admission 20 min after injury, he had no recordable blood pressure, and a tachycardia of 140/min. Following resuscitation with 4000 ml of crystalloid solution and 4 units of blood, a systolic blood pressure of 70 mmHg was recorded 30 min after admission.

Exploration of his thigh revealed injuries to the femoral vein and artery and extensive soft tissue damage. The femur was intact. There were no intra-abdominal injuries. The vessels were repaired and the penile wounds debrided. Intense venous congestion of the calf necessitated four compartment fasciotomy. Postoperatively, a foot pulse was readily palpable and the leg oedema rapidly resolved.

The day after surgery, the patient complained of right iliac fossa pain. There was some local tenderness with diminished bowel sounds and a faecal occult blood test was negative. Abdominal X-ray and intravenous pyelogram were normal. His pain increased and by the third day he was pyrexial (38·8 °C) and had right abdominal rebound tenderness. He had not passed a stool and no blood was passed per rectum. A laparotomy was performed. This revealed gangrene (without perforation) of the caecum, ascending colon and proximal transverse colon, with pulsatile ileocolic and middle colic arteries. There was no other abdominal pathology. A right hemicolectomy with ileocolic anastomosis was performed and the patient made a good recovery. Histological examination of the resected specimen revealed full thickness bowel necrosis. None of the major arteries or veins contained thrombus but minor vessels contained microthrombi.

Discussion

Acute ischaemic colitis is a well described complication of hypotension particularly in elderly patients with occlusive disease of the mesenteric vessels[1,4,5]. It is rare in young previously healthy patients. The commonest presentation is abdominal pain and bleeding per rectum due to mucosal ulceration[1], and full thickness necrosis of the bowel wall is rare. The ten reported cases of gangrenous colon following non-abdominal trauma and systemic hypotension[1,6–8], and the one described following a splenic artery stab[6], were all in patients less than 30 years of age. Seven of the ten patients had full thickness necrosis of at least the right colon[6,7]; one had full thickness caecal necrosis[8] and the remaining two were not clearly documented[1].

In 1939, Penner and Bernheim studied enterocolitis in the acute postoperative phase, and first suggested a link between intestinal ischaemia and infarction secondary to systemic hypotension[9]. Lillehei *et al.* induced haemorrhagic shock in dogs and demonstrated both small and large bowel necrosis after prolonged shock[10]. Following experiments on flow characteristics within the mesenteric circulation when subjected to changing haemodynamics, Nikas *et al.* found that, within the mesenteric circulation, the colon has the greatest sensitivity to hypotension[11].

Theoretically, the section of the gastrointestinal tract most sensitive to ischaemia should be the splenic flexure, where branches of the superior and inferior mesenteric arteries anastomose; yet all the above reported cases, including our own, have involved the right colon (caecum, ascending colon or proximal transverse colon). The ten reported young patients had no primary colonic pathology and no arterial histological changes, so an anatomical abnormality of the mesenteric circulation may account for the right-sided necrosis. Abnormal anastomoses in an area around an absent right colic artery may have been present, but none of the patients was subjected to selective mesenteric angiography.

Abdominal signs following trauma-induced hypotension without abdominal injury warrant careful monitoring and early laparotomy.

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References

1. Sakai L, Keltner R, Kaminski D. Spontaneous and shock-associated ischaemic colitis. *Am J Surg* 1980; **140**: 755–60.
2. Ende N. Infarction of the bowel in cardiac failure. *N Engl J Med* 1958; **18**: 879–81.
3. Blennerhassett JB, Reid JD. Intestinal infarction: with particular reference to cases occurring without macroscopic occulsion of vessels. *NZ Med J* 1960; **59**: 131–8.
4. Marston A. *Intestinal Ischaemia.* Chicago: Year Book Medical Publishers, 1977: 78–9.
5. Ming S. Haemorrhagic necrosis of the gastrointestinal tract and its relation to cardiovascular status. *Circulation* 1965; **32**: 332–41.
6. Flynn TC, Rowlands BJ, Gilliland M, Ward RE, Fischer RP. Hypotension-induced post-traumatic necrosis of the right colon *Am J Surg* 1983; **146**: 715–18.
7. Renton CJC. Massive intestinal infarction following multiple injury. *Br J Surg* 1967; **54**: 399–402.
8. Rickert RR, Johnson RG, Wignarajan KR. Ischemic colitis in a young adult patient. *Dis Colon Rectum* 1974; **17**: 112–16.
9. Penner A, Bernheim AI. Acute postoperative enterocolitis: a study on the pathologic nature of shock. *Arch Pathol Lab Med* 1939; **27**: 966–83.
10. Lillehei RC, Longerbean JK, Bloch JH, Manax WG. The nature of irreversible shock: experimental and clinical observations. *Ann Surg* 1964; **160**: 682–710.
11. Nikas D, Ahn Y, Fielding LP. Sensitivity of colon blood flow to changing haemorrhagic events. *Curr Surg* 1985; **42**: 20–3.

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Actinomycosis of the pancreas

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Abdominal actinomycosis accounts for about 20 per cent of all cases of human actinomycosis[1]. The appendix is most frequently involved. Less commonly the colon, stomach and liver may be the site of infection. Rare sites include the gallbladder and pancreas[2]. Pancreatic involvement is exceptionally rare and we have found only four cases of pancreatic actinomycosis previously described.

Case report

A 57-year-old man was referred to the Hammersmith Hospital with severe right hypochondrial pain and with a provisional diagnosis of pancreatic neoplasm. He had a 10 year history of mild postprandial right hypochondrial discomfort which had become more severe and associated with nausea, vomiting and diarrhoea over the preceding 3–4 months. Two months before presentation this had been accompanied by intermittent pyrexia and a 10 kg weight loss. He had suffered an episode of jaundice of unknown aetiology at the age of 16 and had had appendicectomy 20 years previously. On admission he was apyrexial and not jaundiced but had marked painless hepatomegaly. Laboratory tests including liver function tests and α-fetoprotein were within normal limits. Faecal examination revealed no parasites. Serological tests for *Entamoeba histolytica* and hydatid were negative.

An intravenous cholangiogram was normal. Barium meal showed extrinsic pressure on the gastric antrum and duodenum. Endoscopy confirmed this finding and revealed mild pyloric and proximal duodenal oedema. Barium enema showed external compression at the hepatic flexure. Superior mesenteric artery angiography demonstrated a lesion in the region of the gastroduodenal, pancreaticoduodenal and middle colic arteries displacing the normal vessels; a pathological circulation in some areas was interpreted as suggestive of an inflammatory mass.

Laparotomy revealed an inflammatory mass in the right sub-hepatic space medial to the gallbladder, impinging on the transverse colon and hepatic flexure. The posterior extension was not clearly identified but was anterior to the free edge of the lesser omentum and tracked downwards toward the head of the pancreas. The mass appeared solid without evidence of necrosis. No pus was observed although a few small granules were found deep within the mass. Frozen section revealed chronic non-specific inflammatory granulomatous tissue without evidence of malignancy. A drain was inserted into the mass and the abdomen closed. Recovery was uneventful.

Histological and microbiological examination revealed sparse irregular, interwoven, Gram-positive non-acid fast filaments with branching characteristic of *Actinomyces* species. Aerobic and anaerobic cultures were sterile after 3 weeks incubation. The patient received penicillin 600 mg (6 hourly) and sulphamethoxazole 400 mg plus trimethoprim 80 mg (8 hourly) for 3 months postoperatively. At follow-up 5 years after surgery he was well and free of symptoms.

Discussion

Actinomycosis is a chronic suppurative infection caused by filamentous Gram-positive, non-acid fast micro-aerophilic or anaerobic organisms: *Actinomyces israelii* is the most common species. The main characteristics of the inflammatory process are spread by contiguity, formation of multiple abscesses and draining sinuses and abundant granulation with a dense fibrous reaction[3]. Discharge of 'sulphur granules' composed of dense masses of tightly interwoven filaments is pathognomonic.

Primary pancreatic actinomycosis is rare[4]. The route of infection remains obscure; possibilities include reflux of duodenal contents to the pancreatic duct, silent perforation of adjacent hollow viscera and slowly progressive infection following an episode of acute appendicitis. In this case it seems probable that reflux of duodenal contents contaminated by actinomycetes of oropharyngeal origin had occurred.

Actinomycosis is managed by giving penicillin for extended periods[1,3]. In this case, the addition of sulphonamides was considered appropriate because of failure to isolate the causative organism and of the increased susceptibility of *Nocardia* species to this agent[5]. Differentiation of *Actinomyces* and *Nocardia* infection is generally difficult although the former are more commonly associated with the presence of sulphur granules, a dense fibrotic reaction and absence of central liquefaction or necrosis. Moreover, commonly encountered pathogenic *Nocardia* species are acid-fast. The diagnostic procedures and operative findings in this case suggested an inflammatory aetiology and the primary treatment consisted of surgical drainage. Frozen section, bacteriological and subsequent histological examination suggested pancreatic actinomycosis. Treatment with penicillin and sulphamethoxazole was commenced with an excellent long term result.

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References

1. Drutz DJ. Actinomycosis. In: Wyngaarden JB, Smith LH, eds. *Cecil Textbook of Medicine*. Philadelphia: W.B. Saunders, 1982: 1532–3.
2. Berardi RS. Abdominal actinomycosis. *Surg Gynecol Obstet* 1979; **149**: 257–66.
3. Braude AI. Actinomycosis. In: Braude AI, eds. *Medical Microbiology and Infectious Diseases*. Philadelphia: W.B. Saunders, 1981: 846–50.
4. Weese WC, Smith IM. A study of 57 cases of actinomycosis over a 36 year period. *Arch Intern Med* 1975; **135**: 1562–8.
5. Curry WA. Human nocardiosis: a clinical review with selected case reports. *Arch Intern Med* 1980; **140**: 818–26.

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The dangers of home-brewing: oesophageal rupture

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Blast injury to the oesophagus is rare. Previously reported cases have occurred as a result of rapidly expanding compressed air, methane, carbon monoxide or nitrogen.

Case report

A 29-year-old amateur brewer initiated fermentation in an unvented commercial aluminium beer keg. On unscrewing the plug 8 days later an explosion occurred, hurling him several feet. He developed severe chest pain, haemoptysis and became extremely dyspnoeic. Examination revealed surgical emphysema in the neck and signs of a right tension pneumothorax confirmed radiologically. Emergency treatment included intercostal drainage, nil orally, oxygen by mask and broad spectrum antibiotics.

Further examination revealed superficial facial lacerations, conjunctival hyperaemia, and marked swelling and bruising of the soft palate and tonsillar beds. An injury to trachea or bronchus was suspected. Only after some delay was oesophageal rupture considered and confirmed by a dilute barium swallow.

Forty-eight hours after injury a right thoracotomy revealed much pleural soiling, a 5 cm longitudinal tear through mucus membrane, muscularis and pleura just below the azygos arch. Following thorough debridement the oesophagus was repaired with two layers of interrupted polyglactin and the mediastinal pleura approximated with interrupted catgut.

Three days postoperatively, having commented oral fluids, he became pyrexial, developed a large pleural effusion and drained copious amounts of turbid fluid from which *Klebsiella*, *Escherichia* and *Candida* species were cultured. Repeat dilute barium swallow confirmed dehiscence of the repair and he was submitted to further surgery. By this time (7 days after injury) the tissues were friable, the right lung contracted and there was no sign of the previous polyglactin sutures. The margins of the rent excised, and an all-layers repair with continuous linen performed.

He made good progress, nasogastric feeding was commenced but, 13 days after injury, enteral feed appeared in the chest drainage. Nevertheless feeding was continued and the chest tube withdrawn stepwise. He remains well with no stricture formation 5 months after the accident.

Discussion

This case illustrates the dangers of fermentation in an unvented closed container. The risk of oropharyngeal injury from home-made beer stored under pressure has recently been highlighted in two patients who removed bottle caps with their teeth[1]. The presence of oropharyngeal injury in this patient suggests that the blast wave was directed through the mouth into the upper gastrointestinal tract.

The present case unfortunately demonstrates the problem of delayed diagnosis. The clinical urgency of a large pneumothorax and acute respiratory embarrassment focused attention erroneously on the major airways. Michel, Grillo and Matt report that, of 85 patients with oesophageal rupture, the correct diagnosis was only reached at post-mortem examination in 13 (15 per cent)[2].

Most authors stress the importance of early diagnosis of oesophageal rupture and, although the necessity for early aggressive surgery in all patients has been questioned, there are certain caveats. Firstly, instrumental perforations during fibreoptic endoscopy form a distinct subgroup in whom early 'active conservative' management yields good results[3] but this cannot be extrapolated to other aetiological groups. Secondly, successful conservative management (without drainage) has been described in patients with both cervical and thoracic perforations, but only when confined to the mediastinum with no evidence of pneumothorax, pleural effusion, sepsis, respiratory failure or shock[2].

In general, surgery postponed beyond 12 h is associated with a mortality of up to 50 per cent. With delay the oesophageal wall tends to become friable and will not hold sutures and simple suture alone is associated with a high leakage rate[4].

Delayed diagnosis may not be a contra-indication to attempted repair, although some form of buttressing such as a pedicled pleural flap[2] is probably indicated. Whether or not any procedure more complex than debridement and drainage is undertaken in delayed cases remains debatable.

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References

1. Vallis MD, Gibbon KP. The exploding bottle top and oropharyngeal injuries. *Br J Surg* 1986; **73**: 221.
2. Michel L, Grillo HC, Matt RA. Operative and non-operative management of esophageal perforations. *Ann Surg* 1981; **194**: 57–63.
3. Wesdorp ICE, Bartelsman JFW, Muibregtse K, Den Hartog Jager FCA, Tytgat GM. Treatment of instrumental oesophageal perforation. *Gut* 1984; **25**: 398–404.
4. Abbot OA, Mansour KA, Logan WD *et al.* Atraumatic so-called 'spontaneous rupture of the oesophagus'. A review of 47 personal cases with comments on a new method of surgical therapy. *J Thorac Cardiovasc Surg* 1970; **59**: 67–83.

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Book reviews

Rob and Smith's Operative Surgery. Urology. Fourth edition

W. Scott McDougal. 280 × 220 mm. Pp. 777. Illustrated. 1986. London: Butterworths. £98.00.

For the fourth edition of the urological volume of Rob and Smith's Operative Surgery, the new General Editors, Hugh Dudley and David Carter, have chosen W. Scott McDougal from Nashville, Tennessee to replace D. Innes Williams as the specialist editor. This seems to accord with the trend in the choice of editorship in other volumes of the series, in which increasingly a North American influence is evident. The proportion of British authors in the new edition has diminished from almost one half to less than one-third. It is hard to escape the unpalatable implication that the influence of British surgery at an international level is declining.

The new urological volume is more than a third as large again as its predecessor and more than twice the price. The increased length has been used to advantage. Open surgery for renal stones is covered in much greater detail although it is likely that the next edition will need to give some greater prominence to percutaneous renal operations. All other aspects of urological surgery, both adult and paediatric, receive much more detailed attention. The editors have succeeded in identifying chapters which needed to be radically brought up to date. New authors have been commissioned for new chapters and have also replaced established names. Most contributors have updated their chapters significantly, both in terms of the text, the amount of surgical detail and the number of illustrations. The familiar format has been maintained. Emphasis is on illustrations and the text is used to help guide the reader swiftly and accurately to the important features of pre-, per- and postoperative care. If there is a weak feature of the book it is in the amount of space devoted to endoscopic procedures. Both the instrumentation and techniques could have been updated more radically.

Nevertheless, this new edition should be available worldwide in every hospital where urological surgery is performed. Many surgeons in training, particularly those dedicated to urology, should make a personal investment, secure in the knowledge that they would be in possession of a magnificantly comprehensive manual.

H. N. Whitfield

A Colour Atlas of Minor Surgery

W. F. Walker. 270 × 240 mm. Pp. 199. Illustrated in colour. 1986. London: Wolfe Medical. £60.00.

Minor operations form a large part of a surgeon's workload and it is refreshing to see a book covering this aspect of surgery. In this volume Mr William Walker aims to take the junior surgeon through a series of minor surgical procedures using a large collection of colour photographs and some accompanying text. The author has designed the book to cover a range of medical, general, ophthalmic, orthopaedic, gynaecological and plastic surgical operations. Most common procedures are described but little detail is given to endoscopic work.

The commendable recent trend to produce realistic operative photographs is occasionally marred by blood staining of the operative field and consequent blurring of detail. Occasionally it might have been useful to have an accompanying line drawing to illustrate detail from some of the photographs.

Emphasis is placed on safety and avoidance of surgical pitfalls, details of which are often omitted from other operative surgical descriptions. This book will be useful to the young surgeon both for operative technique and exam revision and although the price is inevitably rather high it should be a welcome addition to the junior surgeon's reading.

M. K. H. Crumplin

Preparation and Revision for the FRCS

W. E. G. Thomas. 235 × 155 mm. Pp. 184 + ix. Illustrated. 1986. Edinburgh: Churchill Livingstone. £12.50.

Mr Thomas has written what can only be described as a new type of book, and it is an exciting innovation. He has made a careful study of the final FRCS examination and from this has set out to review, in note form, the structure and content of each of its parts. The result is a remarkably comprehensive review of the broad areas of surgery which that examination can cover. Tropical hints on how to deal with the written questions, the pattern of the clinical and operative vivas, and the part played by the histological slides and pathological specimens, should help to reduce the mystique of the ordeal and the nervousness of the candidate. There is no doubt at all that this book must become required reading for anyone sitting the exam.

But the book is more than this. As Mr Thomas has stated, the syllabus for the FRCS 'is the field of surgery' and therefore he does not attempt to cover all surgical knowledge. At the same time, while not everyone would agree with the emphasis afforded to all the data which is presented, it is still a remarkably mature synopsis. Each section contains a great deal of surgical teaching which will serve both as a checking list, and occasionally as a jolt, to all surgeons, and this book will be particularly useful to those who are in any way responsible for teaching, whether it is at a postgraduate or undergraduate level. The style, print and technical presentation of the book are good so that it is easy to read and easy to 'find one's place'.

Mr Thomas is to be congratulated on this educational venture. He has set a new style and with it a new standard. This book can certainly be highly recommended and is excellent value for money.

J. E. Trapnell

Reoperative Surgery of the Abdomen

Donald E. Fry. 235 × 155 mm. Pp. 431 + xi. Illustrated. 1986. New York: Marcel Dekker Inc. $83.50.

Surgeons in all specialities recognize the particular and often daunting problems of reoperation be it for recurrent disease or for surgical complications. This multi-author book addresses these problems in the abdomen and the experienced surgeon will recognize many of the situations discussed and will be able to draw consolation from the thought that others have faced similar difficulties, as well as having a useful and practical guide to management.

The editor, Dr Donald Fry, has gathered a group of contributors from the USA (with just one outsider from Germany) and as a consequence there is a slight bias in presentation. I doubt, for example, if many British surgeons would follow the frequent and detailed follow-up and monitoring after colonic resection for cancer advocated in this book even if economics allowed. This section has an up-to-date review of the implantable Infusaid pump for hepatic metastases, though again with no mention of cost which is the limiting factor in its general application in the U.K.

The scope of the book is wide, covering as it does such diverse topics as biliary stricture, reoperation for failed kidney transplant, reoperation for portal hypertension, retroperitoneal tumours and the whole of gastroenterological surgery. There are excellent chapters on the complications of gastric surgery which are well referenced and in this section the British contribution to the literature is more acknowledged that elsewhere in the book. Intra-abdominal abscess is dealt with in separate sections with a surgical and radiological emphasis, and a combined approach (as in the clinical setting) might have been better. Other topics covered under the loose banner of reoperation are the relatively new technique of endoscopic/percutaneous gastrostomy and the well-established procedures of endoscopic sphincterotomy and percutaneous nephrostomy. All in all a well produced and detailed book which can be recommended.

G. Glazer

Correspondence

Testicular torsion

Sir

We read with interest the recent paper by Anderson *et al.* (*Br J Surg* 1986; 73: 847–9) which suggested that patients who develop testicular torsion have an underlying defect in spermatogenesis.

We have recently reported a large series of testicular torsions[1] and in keeping with other reports[2–4] have found at least 30 per cent of patients had experienced recurrent episodes of scrotal pain. We believed that the oligospermia subsequently found in these patients might be due to ischaemic damaged caused by repeated episodes of 'subacute torsion'.

In an attempt to study this theory we have investigated patients undergoing bilateral testicular fixation for recurrent scrotal pain, with hormonal assays and testicular biopsies. Fourteen patients have been investigated so far and we have found only one with evidence of partial maturation arrest in spermatogenesis. Our study continues; however, the early results suggest that those patients who are at risk of developing testicular torsion do not have an underlying cellular defect. We would therefore disagree with the Bristol study and suggest that whilst many patients suffering testicular torsion are subsequently found to be oligospermic this is not due to a pre-existing defect in spermatogenesis.

D. J. Jones
B. T. Morgans*

Royal Air Force Hospital
Ely
Cambridgeshire CB6 1DN
**Princess Alexandra Hospital*
Royal Air Force Wroughton
Swindon
Wiltshire
UK

1. Jones DJ, Macreadie D, Morgans BT. Testicular torsion in the armed services: twelve year review of 179 cases. *Br J Surg* 1986; **73**: 624–6.
2. Chapman RH, Walton AJ. Torsion of the testis and its appendages. *Br Med J* 1972; **1**: 164–6.
3. Williamson RCN. Torsion of the testis and allied conditions. *Br J Surg* 1976; **63**: 465–76.
4. Whitaker RH. Torsion of the testis. *Br J Hosp Med* 1982; **1**: 66–9.

Authors' reply

Sir

We appreciate the interest shown by Squadron Leader Jones and Wing Commander Morgans, but their preliminary results fail to explain the subfertility found in patients with previous unilateral torsion of the spermatic cord. Although intermittent episodes of twisting are common in susceptible testes, subacute torsion is not the only cause of recurrent scrotal pain[1]. In this context it would be helpful to know the age of their 14 patients, the incidence of the 'bell-clapper' anomaly at operation and their criteria for assessing testicular histology. Besides using Johnsen's method to score defects in spermatogenesis[2], we have graded partial maturation arrest according to the percentage of tubules affected. As a result abnormalities were detected in the contralateral testis at the time of torsion in 13 of 20 patients, and the Johnsen score correlated with the subsequent depression of sperm count. Our results are now corroborated by a similar study from the USA, in which 20 of 38 patients had abnormalities in the opposite testis biopsied at the time of the emergency operation[3]. We submit that the evidence of a pre-existing defect in spermatogenesis is clearcut.

J. B. Anderson
M. J. Cooper
R. C. N. Williamson

University Department of Surgery
Bristol Royal Infirmary
Bristol BS2 8HW
UK

1. Yeates WK. Pain in the scrotum. *Br J Hosp Med* 1985; **33**: 101–4.
2. Johnsen SG. Testicular biopsy score count – a method for registration of spermatogenesis in human testes: normal values and results in 335 hypogonadal males. *Hormones* 1970; **1**: 2–25.
3. Hadziselimovic F, Snyder H, Duckett J, Howard S. Testicular histology in children with unilateral testicular torsion. *J Urol* 1986; **136**: 208–10.

Immunorestorative effect of lipid emulsions during total parenteral nutrition

Sir

We read with interest the article by Monson *et al.* (*Br J Surg* 1986; **73**: 843–6), but felt that more detail on the patients studied should have been included. Two important factors were omitted for each group of patients. How recently had the postoperative patients been operated upon? It is known that there is an operative anaesthetic effect on lymphocyte subpopulations which reverts to normal at the end of one week[1,2]. Secondly, the site of the primary lesion and degree of spread, if any, in those patients with neoplasia should be stated as the present authors demonstrated impaired interleukin-2 production in advanced gastrointestinal cancer when compared with localized disease[3].

The variables in surgical immunology and nutrition are sensitive to so many external influences that we feel it is important that communications on these topics identify carefully the study groups investigated. The interpretation of this interesting paper would, we believe, benefit from this extra information.

R. G. Wilson
I. D. A. Johnston

The University of Newcastle upon Tyne
The Medical School
Framlington Place
Newcastle upon Tyne NE2 4HH
UK

1. Hamid J, Bancewicz J, Brown R, Ward C, Irving MH, Ford WL. The significance of changes in blood lymphocyte populations following surgical operations. *Clin Exp Immunol* 1984; **56**; 49–57.
2. Lennard TWJ, Shenton BK, Borzotta A *et al.* The influence of surgical operations on components of the human immune system. *Br J Surg* 1985; **72**: 771–6.
3. Monson JRT, Ramsden C, Guillou PJ. Decreased interleukin-2 production in patients with gastrointestinal cancer. *Br J Surg* 1986; **73**: 483–6.

Authors' reply

Sir

We would entirely agree with the comments of Mr Wilson and Professor Johnston on the variables which may influence the results of immunological investigations in surgical patients, and in particular the effects of recent surgery and the presence of malignancy. It was with these in mind that we attempted to minimize these effects by allowing the patients to serve as their own controls in this cross-over study. However, in answer to the questions posed, none of the postoperative patients investigated in this report received intravenous feeding within a period of ten days after the operation. All patients with malignant disease in this study had primary tumours arising either in the stomach, pancreas or colon, but none were jaundiced at the time of study. Thus, of the six patients with malignant disease who received TPN-L for the first week of feeding, two had localized pancreatic lesions, two had advanced gastric lesions and, of the remaining two, one had a localized colonic lesion and the other localized gastric carcinoma. Of the four patients who received the carbohydrate-based regimen for the first week, three had localized lesions, two of the stomach and one of the colon, and the remaining lesion was an advanced carcinoma of the stomach.

P. J. Guillou
T. G. Brennan
J. Macfie
J. R. T. Monson
Carol Ramsden

St. James's University Hospital
Leeds LS9 7TF
UK

Notices and announcements

Meetings

5–7 March 1987
1987 British Columbia Heart Foundation Symposium
Vancouver, Canada
Information: 1987 British Columbia Heart Foundation Symposium, 801-750 Jervis Street, Vancouver, BC V6E 2A9, Canada

21–24 March 1987
21st Annual Scientific Meeting of the European Society for Clinical Investigation
Elsinore, Denmark
Information: Congress Office, ESCI-87 c/o D. I. Barry, Department of Psychiatry, 06234 Rigshospitalet, 9 Blegdamsvej, DK-2100 Copenhagen Ø, Denmark

23–25 March 1987
International Meeting on Heart Transplantation, Total Artificial Heart and Assist Devices
Brussels, Belgium
Information: E.C.C.O, Rue Vilain XIV 17a, B–1050 Brussels, Belgium

1–3 April 1987
Association of Surgeons of Great Britain and Ireland
Liverpool, UK
Information: Mr B. T. Jackson, Association of Surgeons of Great Britain and Ireland, Royal College of Surgeons, 35/43 Lincoln's Inn Fields, London WC2A 3PN, UK

28 March–4 April 1987
Fifth Cardiosurgical Symposium
Zürs, Austria
Information: Professor M. Deutsch, II. Chirurg. Univ.-Klinik Wien, Spitalgasse 23, A-1090 Vienna, Austria

5–10 April 1987
American Society of Colon and Rectal Surgeons Annual Convention
Washington, DC, USA
Information: Miss H. Gibson, 615 Griswold, 1717 Detroit, MI 48226, USA

6–8 April 1987
Annual Meeting of the American Association for Thoracic Surgery
Chicago, Illinois, USA
Information: American Association for Thoracic Surgery, 13 Elm Street, Manchester, MA 01944, USA

27–28 April 1987
International Symposium on Reoperative Infrarenal Arterial Surgery
Rigshospitalet, State University Hospital, Copenhagen, Denmark
Information: International Symposium on Reoperative Infrarenal Arterial Surgery, Department of Surgery D, Section of Vascular Surgery, Rigshospitalet, State University Hospital, 9 Blegdamsvej, DK-2100 Copenhagen Ø, Denmark

28–30 April 1987
Annual Meeting of The American Laryngological, Rhinological and Otological Society
Denver, Colorado, USA
Information: Dr Roger Boles, President, c/o Lilibet Coe, Administrative Assistant, Kutztown Road, East Greenville, PA 18041, USA

9–15 May 1987
Digestive Disease Week of the American Gastroenterological Association
Chicago, Illinois, USA
Information: Registration Supervisor, Slack Inc., 8900 Grove Road, Thorofare, NJ 08086, USA

10–13 May 1987
Joint Annual Meeting of the American Lung Association, the American Thoracic Society and the Congress of Lung Association Staff
New Orleans, Louisiana, USA
Information: American Thoracic Society, 1740 Broadway, New York, NY 10019, USA

10–13 May 1987
XXII Congress of the European Society for Surgical Research
Aarhus, Denmark
Information: Aarhus Turistforenings Kongresbureau (Convention Bureau), Radhuset, DK-8000 Aarhus C, Denmark

20–23 May 1987
78th Annual Meeting of the American Association for Cancer Research
Atlanta, Georgia, USA
Information: Margaret Foti, American Association for Cancer Research Inc., Temple University School of Medicine, West Building, Room 301, Broad and Tioga Streets, Philadelphia, PA 19140, USA

22 May 1987
British Association of Endocrine Surgeons
Edinburgh, UK
Information: Mr A. W. Goode, Honorary Secretary to the British Association of Endocrine Surgeons, Surgical Unit, The London Hospital, Whitechapel, London E1 1BB, UK

25–28 May 1987
European Society for Therapeutic Radiology and Oncology Sixth Annual Meeting
Lisbon, Portugal
Information: Professor Dr E. van der Schueren, Department of Radiotherapy, Kapucijnenvoer 35, 3000 Leuven, Belgium

10–12 June 1987
69th Meeting of the Endocrine Society
Indianapolis, Indiana, USA
Information: The Endocrine Society, Annual Meeting Office, 428 E Preston Street, Baltimore, MD 21202, USA

10–13 June 1987
Third International Conference on Malignant Lymphoma Current Status and Prospects
Lugano, Switzerland
Information: Dr F. Cavalli, Head Division of Oncology, Ospedale San Giovanni, CH-6500 Bellinzona, Switzerland

15–19 June 1987
Advanced Hepato-Pancreatico-Biliary Surgery
Lund, Sweden
Information: Professor S. Bengmark, Box 5121, S-220 05 Lund 5, Sweden

22–26 June 1987
Peritoneum and Peritoneal Access
Lund, Sweden
Information: Professor S. Bengmark, Professor of Surgery, Box 5121, S-220 05 Lund 5, Sweden

24–28 June 1987
Annual Meeting of the Western Thoracic Surgical Association
Colorado Springs, USA
Information: Western Thoracic Surgical Association, 13 Elm Street, Manchester, MA 01944, USA

7–8 July 1987
Blood Flow '87 (Biological Engineering Society – Blood Flow Group)
University of Leeds, UK
Information: Mr R. Price, Department of Medical Physics, Leeds General Infirmary, Leeds LS1 3EX, UK

31 August–4 September 1987
Surgical Efficiency and Economy
Lund, Sweden
Information: Professor S. Bengmark–SEE, Box 5121, S-220 05 Lund 5, Sweden

9–11 September 1987
Clinical Controversies in Inflammatory Bowel Diseases
Bologna, Italy
Information: Organizing Secretariat, SO.GE.PA.CO. Spa. piazza Constituzione, 5/c, 40128, Bologna, Italy

15–18 September 1987
The British Society of Gastroenterology Jubilee Meeting
London, UK
Information: The Administrative Secretary, The British Society of Gastroenterology, 3 St Andrew's Place, Regent's Park, London NW1 4LB, UK

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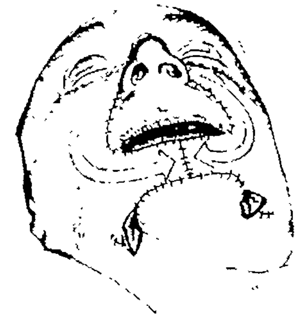

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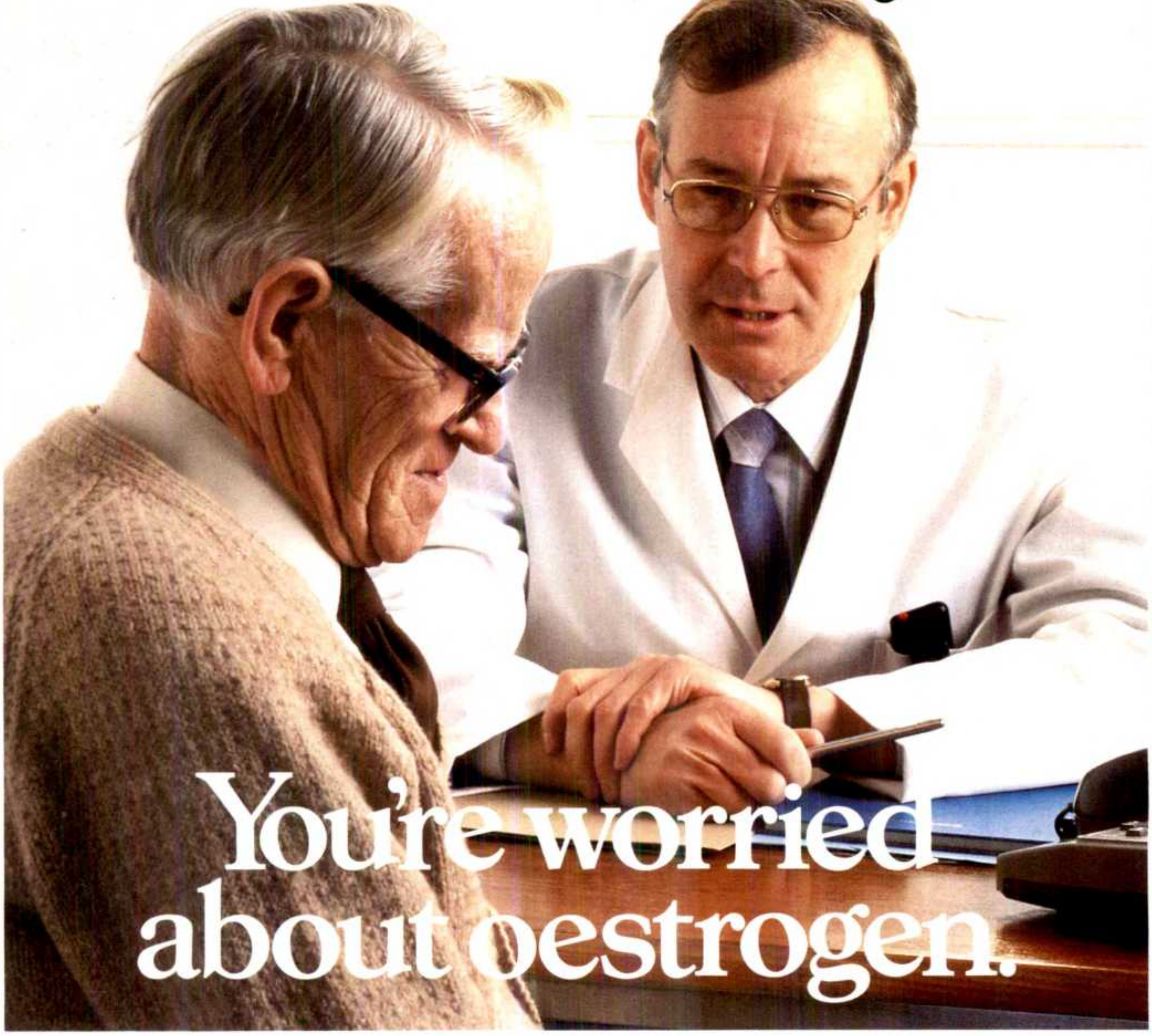
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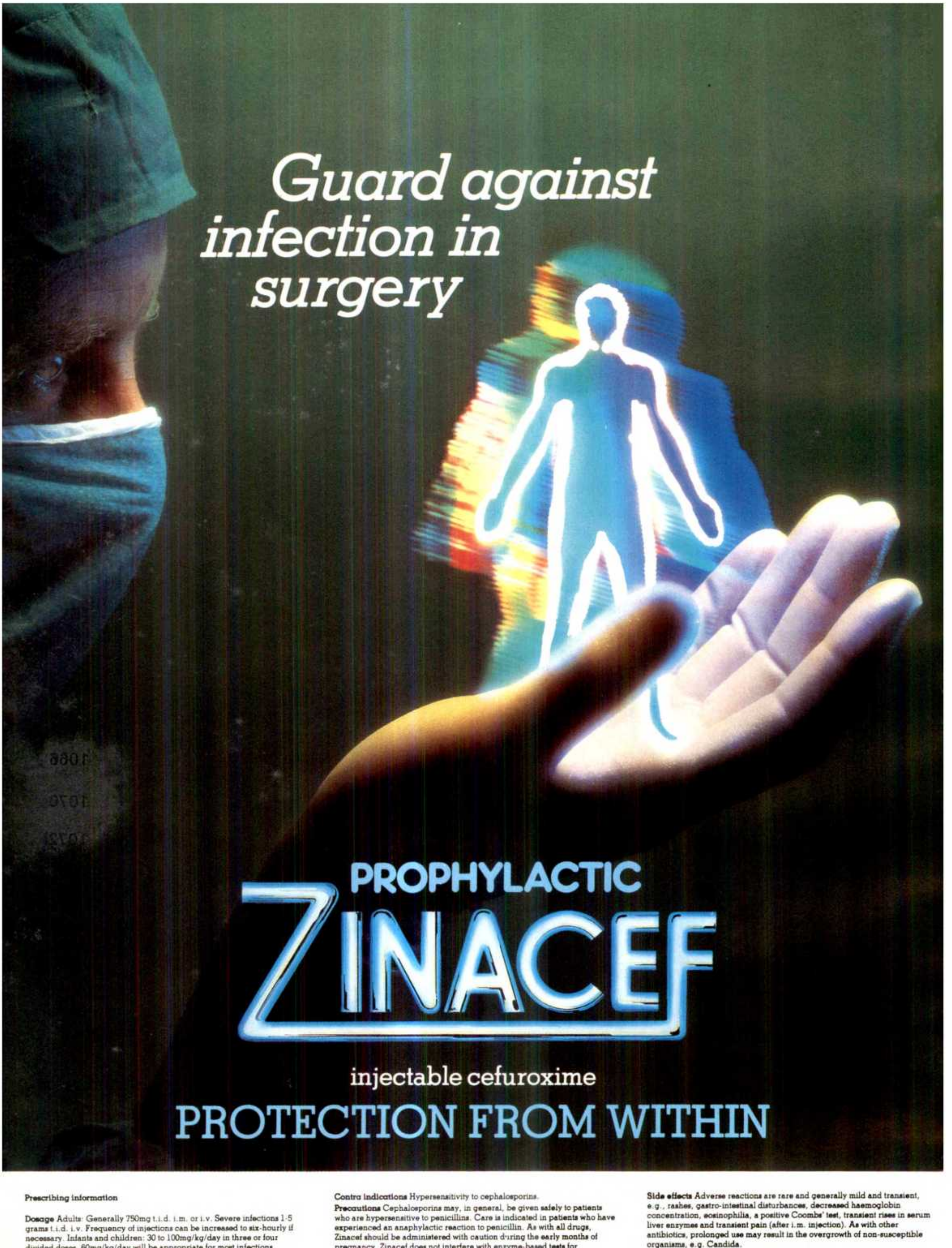

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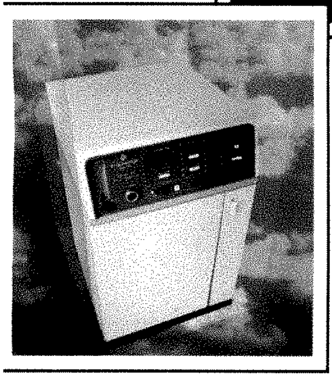

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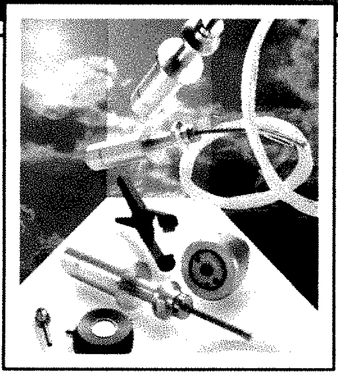

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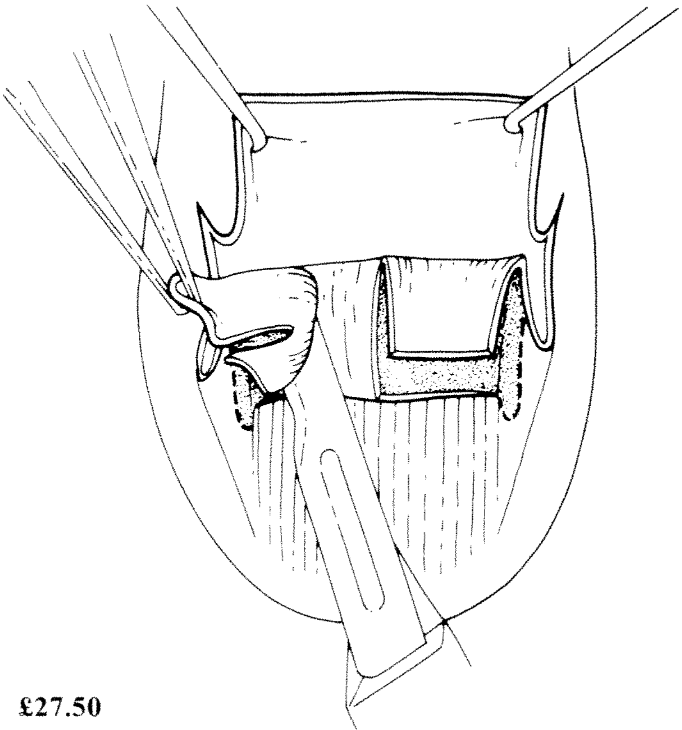

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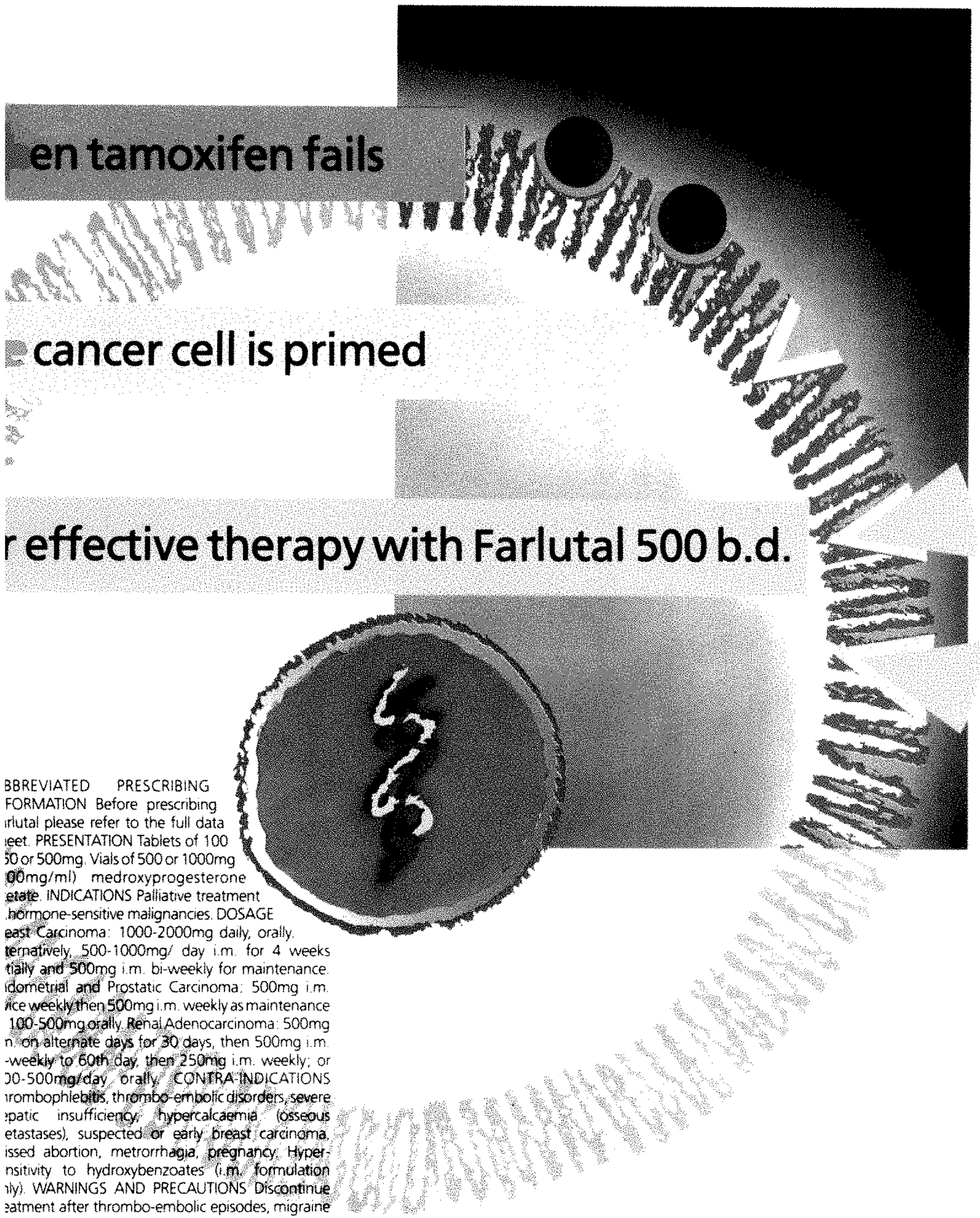

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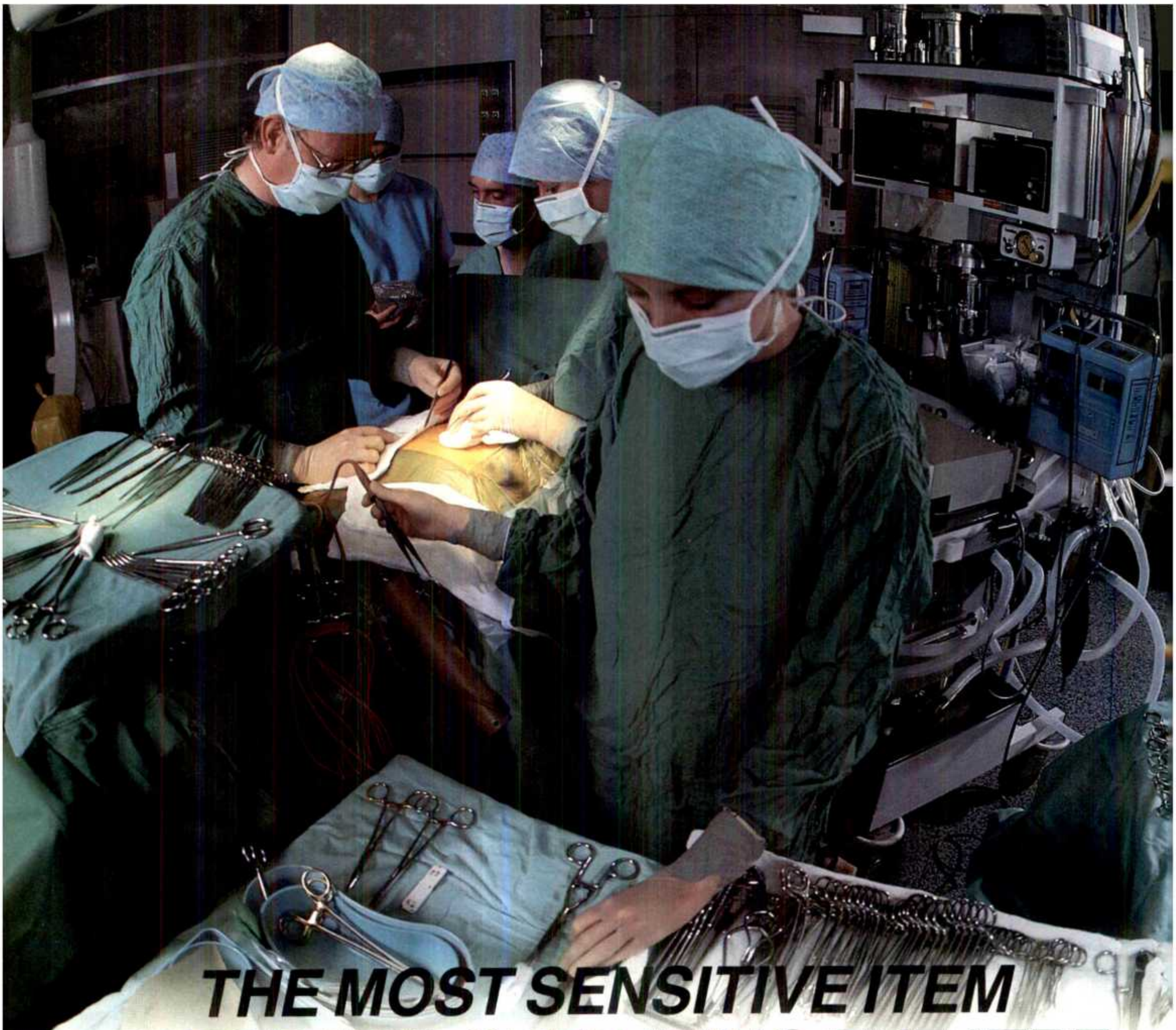

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Br. J. Surg. 1987, Vol. 74, November, 969–970

Non-specific host defence stimulation in the reduction of surgical infection in man

Problems remain, with respect to the control of infection in surgical patients, more than 100 years after the seminal discoveries of Pasteur and Lister. Elective operations continue to carry a 5–7 per cent infection rate despite the wisest possible use of prophylactic antibiotics and optimum sterile technique. Similarly, badly hurt and contaminated patients ultimately manifest infection as the commonest cause of death in a particularly depressing final common pathway of multiple system organ failure. Furthermore, intraperitoneal sepsis remains an incompletely controlled process with a continuing high death rate, particularly in the elderly and in patients whose secondary peritonitis is diagnosed late. It is salutary to note that infection remains the commonest cause of death in the burn patient.

This state of affairs has stimulated many workers to re-examine the age-old proposition of non-specific stimulation of host defence processes. The latest re-emergence of this concept is less than two decades old, and many of the early measures were crude attempts to use agents such as BCG[1] and *Corynebacterium parvum*[2]. Each of those agents provided a degree of protection in highly controlled, carefully conducted experiments simulating surgical infection; the protection was modest and always associated with a reciprocal depression of host defence responses which was dose and/or time related. The discovery and ultimate synthesis of muramyl dipeptide, a defined component of the *Mycobacterium* cell wall, allowed direction of this non-specific stimulus[3]. It is quite clear from the studies of our colleagues at the Institut Pasteur[4] and from our own experience that muramyl dipeptide is a remarkably effective agent which accomplishes, experimentally, many desirable ends, remaining effective in the face of a variety of clinically significant immunodepressant manipulations[5,6]. Furthermore, the agent was shown to be effective, though to a lesser degree, when used for the first time after contamination, and also for polymicrobial sepsis[7,8]. Perhaps most importantly, it was shown to be effective when given in addition to both bacteriostatic and bactericidal antibiotics[9]. Given this remarkable sequence of clinical simulations, one may question why the agent has not moved to bedside trials. An initial clinical trial for the control of post-prostatectomy bacteriuria was promising but, ultimately, no benefit was demonstrated despite considerable concern about the likelihood of type II statistical errors. For whatever reason, the principal patent holder has chosen to focus on the very humane question of its use as an adjuvant to vaccines used for a variety of parasitic diseases in third world countries, and there is little likelihood that it will be promptly assessed for any innate but non-specific benefit in clinical surgery.

As in the elucidation of the ultimate cause of post-traumatic pulmonary insufficiency[10], we decided to turn back to the active trauma services at the University of Louisville Hospitals and begin to examine, in a descriptive and exploratory fashion, the host defence abnormalities in badly injured man. The results of these studies have been widely debated and have provoked several efforts to repeat them in laboratories around the world. Suffice it to say that detailed testing of badly injured man in our principal teaching hospital disclosed only two primary abnormalities that appeared to be independent variables[11]. The first was the capacity of the hosts' monocytes to present antigens appropriately for processing. This antigen-presenting activity was sharply depressed shortly after injury in patients destined to develop severe and frequently fatal infection; it remained depressed for long periods even in those patients ultimately likely to recover from infection. Indeed, recovery correlated very precisely with the return of this monocyte activity toward normal. The second independent variable identified and confirmed has been the tendency of patients' serum to show depressed ability to support phagocytosis by normal neutrophils. Indeed, both extremes of opsonization have been informative; some patients have recovered after repeated bacterial challenges, manifesting clear-cut evidence of a 'super serum' activity, while patients prone to progressive and/or fatal infection demonstrated

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subnormal responses in terms of the capacity of their serum to opsonize test bacteria by normal neutrophils.

The monocyte abnormalities led to a bench pursuit of those methods likely to enhance them, and it is quite clear that *in vitro*, lipopolysaccharide (S. H. Appel, S. T. Wellhausen, M. J. Hershman and H. C. Polk Jr, unpublished data) is consistently capable of stimulating monocyte antigen-presenting activity into the normal range, parenthetically reinforcing the suspicion that under certain circumstances muramyl dipeptide, with its lipopolysaccharide-like activity, remains a highly promising therapeutic possibility. *In vitro* studies have also shown the consistent ability of interferon gamma (IFN-γ) to stimulate macrophage and monocyte activity (M.J. Hershman, S. H. Appel, S. T. Wellhausen, G. Sonnenfeld and H. C. Polk Jr, unpublished data). In a sequence of studies as yet unpublished, *in vivo* IFN-γ has shown consistent effectiveness in surgical models when used for prophylaxis and for therapy, and under conditions of polymicrobial bacterial sepsis. This protective effect in terms of degree of bacteraemia and, indeed, survival was constant and statistically significant but always small! The prospects for a clinical trial are at least dampened by the realization that such an undertaking in the face of only small benefits may well lead to falsely negative clinical results. In theory, the ideal application of this concept, which has a sound classical immunological basis, as well as a sound laboratory background, would be the sequential use of IFN-γ, muramyl dipeptide and possibly tumour necrosis factor[12], with the likelihood that there could be sustained enhancement of host defences until the septic challenge was overcome.

In any event, non-specific enhancement of host defences has been an active and rewarding field of inquiry; it is likely that some or many of the concepts generated will find their way to the bedside, assuming that the early experimental results can be repeated by other groups in a consistent fashion.

H. C. Polk Jr

University of Louisville School of Medicine
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1. Rouben D, Fagelman K, McCoy M, Polk HC Jr. Enhancement of nonspecific host defenses against local bacterial challenge. *Surg Forum* 1977; **28**: 44–5.
2. Polk HC Jr, Calhoun K, Trachtenberg L, Hart K. *Corynebacterium parvum*: Immunomodulation in local bacterial infections. *Surgery* 1980; **87**: 52–8.
3. Chedid L, Parant M, Parant F *et al.* Enhancement of nonspecific immunity to *Klebsiella pneumoniae* infection by synthetic immunoadjuvant (N-acetyl-muramyl-L-alanyl-D-isoglutamine) and several analogs. *Immunology* 1977; **47**: 2089–93.
4. Parant M. Biologic properties of a new synthetic adjuvant, muramyl dipeptide (MDP). *Springer Semin Immunopathol* 1979; **2**: 101–18.
5. Galland RB, Heine KJ, Polk HC Jr. Nonspecific stimulation of host defenses against bacterial challenge in immunosuppressed mice. *Arch Surg* 1983; **118**: 333–7.
6. Galland RB, Polk HC Jr. Non-specific stimulation of host defenses against a bacterial challenge in malnourished hosts. *Br J Surg* 1982; **69**: 665–8.
7. Ausobsky JR, Trachtenberg LS, Polk HC Jr. Enhancement of nonspecific host defenses against combined local bacterial challenge. *Surg Forum* 1982; **33**: 46–7.
8. Ausobsky JR, Cheadle WG, Brosky BC, Polk HC Jr. Muramyl dipeptide increases tolerance to shock and bacterial challenge. *Br J Surg* 1984; **71**: 151–3.
9. Polk HC Jr, Galland RB, Ausobsky JR. Nonspecific enhancement of resistance to bacterial infection. Evidence of an effect supplemental to antibiotics. *Ann Surg* 1982; **196**: 436–41.
10. Fulton RL, Jones CE. The cause of post-traumatic pulmonary insufficiency in man. *Surg Gynecol Obstet* 1975; **140**: 179–86.
11. Polk HC Jr, George CD, Wellhausen SR *et al.* A systematic study of host defense processes in badly injured patients. *Ann Surg* 1986; **204**: 282–99.
12. Parant M, Parant F, Vinit MA, Chedid L. Protective effect of recombinant human tumor necrosis factor against bacterial and fungal experimental infections. *C R Acad Sci Paris* 1987; **304**: 1–4.

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Parietal cell vagotomy: long-term follow-up studies

By the First World War the operative mortality for elective peptic ulcer surgery in some centres was strikingly low, perhaps acceptable by today's standards. Moynihan reported a mortality of 0·5 per cent for gastro-enterostomy in a series of over 500 ulcer patients, and W. J. Mayo described a mortality of 1 per cent in a series of 2700. However, recurrence rates of up to 40 per cent for gastro-enterostomy in duodenal ulcer patients were eventually recorded, and the operation was largely abandoned. It was replaced by Polya gastrectomy, and the more aggressive assault on acid pepsin secretion undoubtedly reduced recurrence but at the price of increased surgical mortality and morbidity produced by the often incurable problems of dumping, bilious vomiting and, to a lesser extent, diarrhoea. Half a century later these side effects are rarely encountered with parietal cell vagotomy, but at what cost in terms of an increased incidence of recurrent ulcer?

In this issue of the Journal, Hoffman, Olesen and Jensen describe their experience of parietal cell vagotomy (pages 1056–9). Now, 18 years after surgeons from this centre of excellence produced one of the original descriptions of the operation, the results obtained at 14–18 year follow-up of 106 patients are presented. A total of 30 per cent had proven symptomatic recurrences, and a further 9 per cent were symptomatic and might have had recurrences but were not examined gastroscopically. There was no operative mortality and no subsequent deaths from ulcer related problems. The 32 recurrent ulcers developed between 2 months and 16 years postoperation, with a mean interval to recurrence of 7 years. Only 30 per cent of the recurrences occurred within 5 years, 40 per cent developed after more than 10 years, and more will probably occur with time. These recurrences were related neither to the anatomical site of the original ulcer nor to the seniority of the surgeon. No asymptomatic ulcers were detected as follow-up endoscopy was not routinely employed; experience gained from other studies would suggest that as many again might have been overlooked[1]. After parietal cell vagotomy only one serious bleed occurred and there were no perforations although, pre-operatively, 37 patients had one or other of these life threatening complications.

Few studies of peptic ulcer surgery have follow-up in excess of 5 years, though those in which parietal cell vagotomy was employed with assessment between 5 and 12 years report incidences of 11, 10, 28, 13, 11·4 and 25·3 per cent in a total of 1258 patients[2–6]. It is likely, therefore, that the patients in other studies with shorter follow-up will develop recurrent ulcers in increasing numbers in the years to come. Rates of ulcer recurrence after parietal cell vagotomy vary widely at 5 years, from 1 per cent[7] to over 25 per cent[4]. The high rates of long-term symptomatic recurrence reported in some series are as bad as, and possibly worse than, those on which gastro-enterostomy alone was discredited.

Why is parietal cell vagotomy failing? In order to heal ulcers and maintain ulcer healing, acid secretion must be reduced to an acceptably low level in the presence of normal or near normal gastric emptying, but the level has never been determined exactly. The aphorism of Schwartz, 'no acid—no ulcer', holds as true today as when enunciated over 70 years ago. Achlorhydria, however, is rarely achieved by vagotomy and would represent a worrying 'overkill'. Perhaps the aphorism 'no vagus—no ulcer' should be the expedient as, in the absence of the rare Zollinger–Ellison syndrome or a delay in gastric emptying, it would appear to hold good. Although complete parietal cell denervation is frequently achieved in the early stages after parietal cell vagotomy it is rarely maintained in the long-term and, after 5 years, most insulin tests have become positive. The significance and mechanism of a late positive insulin response and its relation to recurrent ulcer are ill understood. Recurrences after truncal vagotomy and drainage usually occur within 2 years, but this is not true of parietal cell vagotomy.

Could the operation be ill conceived in that it fails to take account of nerve regeneration, or because the degree of muscular denervation of the proximal stomach is too great? Nerve regeneration, by sprouting from the antral and/or oesophageal mucosal plexuses is theoretically possible, while proximal gastric inertia could be important even in the presence of a functioning antral mill. Ill conceived and

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unnecessary as Holle's suggestion of additional pyloroplasty might seem, it may confer some protection from gastric stasis. Undoubtedly, the major reason for early ulcer recurrence after parietal cell vagotomy is a failure of the technique. The inexperienced surgeon is more likely to fail to achieve: distal denervation at the antral–corpus junction; proximal denervation at the oesophagogastric junction (particularly posteriorly); or oesophageal clearance of small vagal strands. Late recurrence may relate to problems of motility.

Wherein lines the logical solution? Should we abandon elective ulcer surgery or be more selective in its use? Should we use intra-operative testing, or modify parietal cell vagotomy by adding a pyloroplasty or ligating the gastro-epiploic vessels at the antral–corpus junction? Should we adopt a more aggressive or otherwise redesigned surgical approach, or confine ulcer surgery to specialized centres of excellence?

There is still a place for elective peptic ulcer surgery. Although a 1 month course of an H_2 receptor antagonist heals 70 per cent of ulcers and a 2 month course heals about 85 per cent, 90 per cent of these ulcers recur within 1 year of stopping these drugs, however long they have been continued. Even on low dose maintenance therapy the relapse rate is 2·5 per cent per month and 30 per cent per year. While the number of days spent in hospital and operations undertaken because of peptic ulceration have fallen dramatically, and even though the prevalence of the diathesis is falling, there has been no coincident fall in ulcer mortality.

The concept of selecting elective ulcer operations according to pre-operative acid output is an old one. Recurrence rates after highly selective vagotomy do not correlate with pre-operative acid output under either basal or stimulated conditions, and no other predictive indices have consistently emerged which might be suitable as a basis of selection. Intra-operative testing has been shown to reduce the incidence of incomplete vagotomy and, though time consuming, could perhaps be recommended particularly to the surgical trainee.

A recent controlled trial[8] has compared parietal cell vagotomy with and without pyloroplasty and reported a lower recurrence, 8 per cent compared with 20 per cent, in the pyloroplasty group. This difference could increase with time and the question is worthy of further consideration. Dividing the gastro-epiploic vessels at the antral–corpus junction is a simple addition which also needs further evaluation. Peptic ulceration remains a common problem and it would be a retrograde step to recommend that its surgery should be confined to specialized centres. A more aggressive surgical approach could only be justified if the incidence of dumping and diarrhoea could be kept low. Perhaps we should be looking towards techniques which either combine parietal cell vagotomy with mucosal antrectomy[9] or provide complete gastric mucosal vagotomy with preservation of the vagal innervation of the gastric musculature.

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1. Muhe E, Muller C, Martinoli S *et al.* Five years results of a prospective multicentre trial of proximal gastric vagotomy. In: Baron JH, Alexander-Williams J, Allgöwer M, Muller C, Spencer J, eds. *Vagotomy in Modern Surgical Practice.* London: Butterworths, 1982: 176–86
2. Blackett RL, Johnston D. Recurrent ulceration after highly selective vagotomy for duodenal ulcer. *Br J Surg* 1981; **68**: 705–9.
3. De Miguel J. Selective gastric vagotomy and drainage, and highly selective vagotomy for duodenal ulcer. Comparative long term results. In: Baron JH, Alexander-Williams J, Allgöwer M, Muller C, Spencer J, eds. *Vagotomy in Modern Surgical Practice.* London: Butterworths, 1982.
4. Kronborg O. Clinical results 6–9 years after selective and proximal gastric vagotomy for duodenal ulcer. In: Baron JH, Alexander-Williams J, Allgöwer M, Muller C, Spencer J, eds. *Vagotomy in Modern Surgical Practice.* London: Butterworths, 1982: 158–60.
5. Jensen HE, Kjaergaard J, Meissner S. Ulcer recurrence two to twelve years after parietal cell vagotomy for duodenal ulcer. *Surgery* 1983; **94**: 802–6.
6. Teichmann RK, Capeller WA, Kramling HJ, Pratschke E. 10-Jahres-Ergebnisse nach proximal selektiver Vagotomie beim ulcus duodeni-Leiden. Eine prospektive Studie. *Chirurg* 1985; **56**: 515–20.
7. Fraser AG, Brunt PW, Matteson NA. A comparison of highly selective vagotomy and truncal vagotomy and pyloroplasty—one surgeon's results after 5 years. *Br J Surg* 1983; **70**: 485–9.
8. Emas S, Fernström M. Prospective randomized trial of selective vagotomy with pyloroplasty and selective proximal vagotomy with and without pyloroplasty in the treatment of duodenal pyloric and prepyloric ulcers. *Am J Surg* 1985; **149**: 236–43.
9. Becker JM, Kelly KA, Haddad AC, Zinsmeister AR. Proximal gastric vagotomy and mucosal antrectomy: a possible operative approach to duodenal ulcer. *Surgery* 1983; **94**: 58–64.

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Postoperative intra-abdominal sepsis

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Postoperative intra-abdominal sepsis carries a high mortality. Diagnosis by clinical examination is often difficult, and imaging techniques may be helpful. Diagnostic laparotomy should be considered early, even in the absence of localizing signs. The use of aggressive surgical techniques may improve prognosis. The timing of surgical intervention is as important as the technique. Early diagnosis and treatment is particularly crucial in critically ill patients.

Keywords: Intra-abdominal sepsis, postoperative complications, laparotomy, multiple organ failure

Intra-abdominal sepsis (IAS) which persists or develops postoperatively carries a high mortality and morbidity[1–4]. The diagnosis may be missed altogether[5] or delayed to the extent that irreversible clinical deterioration occurs[4]. Early recognition and prompt treatment may be impeded by a lack of classical localizing signs and, in the absence of such signs, by a reluctance to embark on a diagnostic laparotomy in a critically ill patient.

Postoperative IAS may result from severe disseminated primary infection, inadequate primary treatment, anastomotic breakdown, or depressed host defence. Although this problem may be infrequently encountered in any particular surgeon's practice (only 1·6 per cent of almost 5000 laparotomies reported by Hinsdale and Jaffe[4]) it is a common cause of admission to an intensive therapy unit (5 per cent of all admissions to the Intensive Therapy Unit of the Western Infirmary, Glasgow, in 1986). It is particularly common after certain types of surgery, for example laparotomy for septic complications of diverticular disease which may carry a mortality due to sepsis of 23 per cent[6], or laparotomy for penetrating abdominal trauma after which abscess formation occurs in 2·4–12 per cent[7,8].

Diagnosis

After a laparotomy sepsis may present with a combination of some or all of the following features: a high or low temperature, tachycardia, hypotension, pulmonary or systemic oedema, hyperventilation with hypocapnia, mental confusion, an elevated or reduced white blood cell count, and a falling platelet count with or without evidence of disseminated intravascular coagulation[9]. The septic focus is usually to be found in the lungs, urinary tract or abdomen. Clinical examination and the appropriate laboratory investigations will usually identify respiratory, urinary or other sources of infection, but the diagnosis of intra-abdominal sepsis is often more difficult.

Clinical signs are non-specific and may be masked in the postoperative patient[1]. Abdominal tenderness, pyrexia and ileus are almost universal accompaniments of intra-abdominal sepsis[4] but may present postoperatively for reasons other than sepsis. A high index of suspicion should therefore be maintained, and all patients who fail to progress postoperatively, or show evidence of sepsis or remote organ failure, without obvious cause, should have intra-abdominal sepsis excluded.

Plain abdominal X-rays may reveal gas or a gas–fluid interface in an abscess. Contrast studies may reveal organ displacement due to fluid collections, or may confirm the presence and site of anastomotic dehiscence. Persistent lower lobe atelectasis and effusion on a chest X-ray may indicate the presence of a subphrenic collection. In general, such techniques have a low sensitivity and specificity.

Diagnostic accuracy is improved by the use of modern scanning techniques. Ultrasound (US) and computed tomography (CT) are the most useful investigative techniques in this field with accuracies of 60–90 per cent in the case of ultrasound[10–12] and over 90 per cent for CT scanning[13–17]. Gallium and indium scans are less helpful but may contribute useful information in some patients[18]. Several authors have commented on the complementary nature of multiple investigations[18–20]. The published accuracy of these investigations does not always give a guide to their clinical usefulness because the reports are often not sufficiently definite to allow a decision on further surgery to be made.

Where clinical suspicion of intra-abdominal sepsis is high, diagnostic laparotomy should be considered despite negative results from imaging techniques[21–23]. As a rule, the sicker the patient the stronger the indication for early laparotomy. Careful pre-operative preparation of the patient should not be omitted in the interest of haste, but once initial resuscitation has been carried out, delay will lead only to deterioration; early diagnosis and treatment are mandatory[24,25].

Treatment

The mainstay of treatment of intra-abdominal sepsis is drainage of the septic focus, together with removal of any continuing source of infection if feasible[26]; parenteral antibiotics have an important adjunctive role. A collection of pus may be drained in three ways: transperitoneally, extraperitoneally and percutaneously under CT or US guidance. The transperitoneal route has the advantage that infection does not need to be localized pre-operatively, and multiple foci or disseminated infection can be drained. It may be technically difficult and the integrity of the bowel may be breached while dividing dense adhesions[27]. The extraperitoneal route has similar advantages and disadvantages to percutaneous needle drainage. It requires precise localization of the infective focus, but causes less blood loss and the bowel is entered less often[27,28]. If the infection is localized, and the patient haemodynamically stable, an extraperitoneal or needle drainage approach is justified. Where the patient is unstable and imaging procedures would merely delay treatment, especially if multiple foci or disseminated infection is suspected, then the transperitoneal approach should be used[27].

Peritoneal lavage as an adjunct to debridement at laparotomy was advocated at the beginning of this century but fell into disrepute in the mistaken belief that it encouraged

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dissemination of otherwise localized infection. In 1972 in a study in dogs, Hovnanian[29] demonstrated that this was not the case and intra-operative lavage is now widely accepted as being beneficial. The value of adding antibiotics to the lavage fluid however has not been satisfactorily demonstrated. Several experimental studies[30–32] have failed to demonstrate any added benefit of antibiotics in lavage fluid provided suitable parenteral antibiotics are administered. In clinical practice good results with antibiotic lavage have been reported[33,34] but comparative studies are lacking and its benefit remains unproven. Continuation of lavage postoperatively has also been advocated[33] but it seems likely that drains placed for this purpose at laparotomy are quickly walled off and lavage of the whole abdomen is not possible[35].

Despite apparently adequate surgery the mortality from this condition remains depressingly high[36]. In an effort to improve this dismal outlook several aggressive surgical approaches have been proposed. In an uncontrolled personal study of radical peritoneal debridement, Hudspeth reported good results[37], but a subsequent randomized trial of this same technique by Polk and Fry showed no benefit[38]. The radical operation in Polk's study was universally fatal in patients over 60 years of age—clearly raising serious doubts about the uncritical application of this technique.

Since 1979 some authors have described open drainage of the peritoneal cavity[39–42] and interest in this approach has recently increased[43–45]. Formal closure of the abdomen is said to be associated with a high incidence of recurrent sepsis and the proponents of open drainage or 'laparostomy' suggest that free drainage of pus is possible if the abdomen is left open and repeated peritoneal lavage and exploration are facilitated. Bradley *et al.*[43] demonstrated a mortality of 23 per cent in patients treated by open drainage compared with 44 per cent in those treated by closed drainage, but this study used historical controls. A modification of the open drainage technique has been described by Hedderich *et al.*[35]. The defect in the abdominal wall is closed by a sheet of polypropylene mesh stitched to the wound edges; a zipper is incorporated in the polypropylene and this can be opened to permit frequent peritoneal lavage and gentle exploration to break down pockets of pus. In a series of ten patients this method led to survival in eight. Andrus *et al.*[46], however, demonstrated no benefit from planned daily laparotomies in patients with IAS compared with a matched control group who had further operations only when recurrent sepsis was suspected. It should be pointed out however that, even in the control group, the reoperation rate was higher than in similar series reported by other surgeons equally interested in IAS[27,47,48]. Further controlled trials are necessary; in the meantime, reoperation on suspicion of continuing sepsis is appropriate. If frequent laparotomy becomes necessary, the trauma of repeated operation may be minimized by open drainage or the use of a zipper technique.

The mortality of postoperative IAS remains high despite recent advances in understanding of its aetiology and more aggressive and radical treatment. Two approaches can be recommended currently to reduce this mortality. Firstly, prevention of postoperative IAS may be possible. The colon is the source of contamination in 30–50 per cent of cases of IAS[3,49]. A meticulous diagnostic and surgical approach to primary colonic surgery by experienced surgeons reduces postoperative septic complications[26,49] and a more widespread application of these practices is indicated. Secondly, if IAS is suspected, diagnostic and therapeutic efforts should be applied early; in the presence of organ failure, surgery within 24 hours is associated with improved survival[3].

A variety of treatment regimens is described above; none is clearly superior. Assessment of published work is hampered by the uncontrolled nature of many of the studies. A number of scoring systems such as the sepsis score[50], the APACHE II score[51] and the surgical infection stratification system[48] have been devised to aid audit and comparison between groups of patients. Future trials should include the use of such scoring systems; Dellinger's surgical infection stratification system is objective, simple, and is based on the APACHE II score which has been validated in thousands of critically ill patients, and it appears to be the most useful scoring system in this context[48].

In conclusion, postoperative IAS is a common cause of admission to the intensive therapy unit and, despite recent advances in surgery and intensive care, mortality is high. If IAS is suspected, particularly if clinical deterioration is associated with the onset of haemodynamic instability, surgical intervention should be urgently considered if organ failure is to be avoided. After prompt resuscitation, diagnostic and therapeutic laparotomy should be considered sooner rather than later, the precise technical details being less important than the decision to operate. It is often said that a patient is too unwell for an operation in these circumstances. The converse is true; the sicker the patient, the more urgent his need[3,24,25].

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References

1. Le Gall JR, Fagniez PL, Meakins J, Buisson CB, Trunet P, Carlet J. Diagnostic features of early high post-laparotomy fever; a prospective study of 100 patients. *Br J Surg* 1982; **69**: 452–5.
2. Pitcher WD, Musher DM. Critical importance of early diagnosis and treatment of intra-abdominal infection. *Arch Surg* 1982; **117**: 328–33.
3. Bohnen J, Boulanger M, Meakins JL, McLean APH. Prognosis in generalised peritonitis: relation to cause and risk factors. *Arch Surg* 1983; **118**: 285–90.
4. Hinsdale JG, Jaffe BM. Reoperation for intra-abdominal sepsis. *Ann Surg* 1984; **199**: 31–6.
5. Bell RC, Coalson JJ, Smith JD, Johansen WG. Multiple organ system failure and infection in adult respiratory distress syndrome. *Ann Intern Med* 1983; **99**: 293–8.
6. Lambert ME, Knox RE, Schofield PF, Hancock BD. Management of the septic complications of diverticular disease. *Br J Surg* 1986; **73**: 576–9.
7. Gibson DM, Feliciano DU, Mattox KL, Gentry LO, Jordan GL. Intra-abdominal abscess after penetrating abdominal trauma. *Am J Surg* 1981; **142**: 699–703.
8. Pilcher DB. Penetrating injuries of the liver in Vietnam. *Ann Surg* 1969; **170**: 793–800.
9. Ayres SM. SCCM's new horizons conference on sepsis and septic shock. *Crit Care Med* 1985; **13**: 864–6.
10. Doust BD, Doust VL. Ultrasonic diagnosis of abdominal abscesses. *Dig Dis Sci* 1976; **21**: 569–76.
11. Richardson R, Norton LW, Eule J, Eiseman B. Accuracy of ultrasound in diagnosing abdominal masses. *Arch Surg* 1975; **110**: 933–9.
12. Hill BA, Yamaguchi K, Flynn JJ, Miller DR. Diagnostic sonography in general surgery. *Arch Surg* 1975; **110**: 1089–94.
13. Saini S, Kellum JM, O'Leary MP *et al.* Improved localization and survival in patients with intra-abdominal abscesses. *Am J Surg* 1983; **145**: 136–42.
14. Wolverson MK, Jagannadharao B, Sundaram M, Joyce PF, Riaz MA, Shields JB. CT as a primary diagnostic method in evaluating intra-abdominal abscess. *AJR* 1979; **133**: 1089–95.
15. Haaga JR, Alfidi RJ, Havrilla TR *et al.* CT detection and aspiration of abdominal abscesses. *AJR* 1977; **128**: 465–74.
16. Robison JG, Pollock TW. Computed tomography in the diagnosis and localisation of intra-abdominal abscesses. *Am J Surg* 1980; **140**: 783–6.
17. Koehler PR, Knochel JQ. Computed tomography in the evaluation of abdominal abscesses. *Am J Surg* 1980; **140**: 675–8.
18. Polk HC, Lamont PM. The search for pus. *Br J Hosp Med* 1983; **30**: 199–202.
19. Shimshak RR, Korobkin M, Hoffer PB, Schor R, Hill TC, Kressel HY. The complementary role of gallium citrate imaging and computed tomography in the evaluation of suspected abdominal infection. *J Nucl Med* 1978; **19**: 262–9.

20. Joseph AEA. Imaging of abdominal abscesses. *Br Med J* 1985; **291**: 1446–7.
21. Polk HC, Shields CL. Remote organ failure: a valid sign of occult intra-abdominal infection. *Surgery* 1977; **81**: 310–13.
22. Eiseman B, Beart R, Norton L. Multiple organ failure. *Surg Gynecol Obstet* 1977; **144**: 323–6.
23. Fry DE, Pearlstein L, Fulton RL, Polk HC. Multiple system organ failure. *Arch Surg* 1980; **115**: 136–40.
24. Meakins JL, Wicklund B, McLean APH. The surgical intensive care unit; current concepts in infection. *Surg Clin N Am* 1980; **6**: 117–32.
25. Nel CJC, Pretorius DJ, De Vaal JB. Re-operation for suspected intra-abdominal sepsis in the critically ill patient. *S Afr J Surg* 1986; **24**: 60–2.
26. Koruth NM, Hunter DC, Krukowski ZH, Matheson NA. Immediate resection in emergency large bowel surgery: a 7 year audit. *Br J Surg* 1985; **72**: 703–7.
27. Stone HH, Mullins RJ, Dunlop WE, Strom PR. Extraperitoneal versus transperitoneal drainage of the intra-abdominal abscess. *Surg Gynecol Obstet* 1984; **159**: 549–52.
28. Gerzof SG, Robbins AH, Johnson WC, Berkett DH, Nabseth DC. Percutaneous catheter drainage of abdominal abscesses. *N Engl J Med* 1981; **305**: 653–7.
29. Hovnanian AP, Saddawi N. An experimental study of the consequences of intraperitoneal irrigation. *Surg Gynecol Obstet* 1972; **134**: 575–8.
30. Hau T, Nishikawa R, Phuangsab A. Irrigation of the peritoneal cavity and local antibiotics in the treatment of peritonitis. *Surg Gynecol Obstet* 1983; **156**: 25–30.
31. Lally KP, Trettin JC, Torma MJ. Adjunctive antibiotic lavage in experimental peritonitis. *Surg Gynecol Obstet* 1983; **156**: 605–8.
32. McAvinchey DJ, McCollum PT, Lynch G. Towards a rational approach to the treatment of peritonitis: an experimental study in rats. *Br J Surg* 1984; **71**: 715–17.
33. Stephen M, Loewenthal J. Continuing peritoneal lavage in high risk peritonitis. *Surgery* 1979; **85**: 603–6.
34. Krukowski ZH, Koruth NM, Matheson NA. Antibiotic lavage in emergency surgery for peritoneal sepsis. *J R Coll Surg Edinb* 1986; **31**: 1–6.
35. Hedderich GS, Wexler ML, McLean APH, Meakins JL. The septic abdomen: open management with Marlex mesh with a zipper. *Surgery* 1986; **99**: 399–408.
36. Norton LW. Does drainage of intra-abdominal pus reverse multiple organ failure? *Am J Surg* 1985; **149**: 347–50.
37. Hudspeth AS. Radical surgical debridement in the treatment of advanced generalized peritonitis. *Arch Surg* 1975; **110**: 1233–6.
38. Polk HC, Fry DE. Radical peritoneal debridement for established peritonitis. *Ann Surg* 1980; **192**: 350–5.
39. Steinberg D. On leaving the peritoneal cavity open in acute generalised suppurative peritonitis. *Am J Surg* 1979; **137**: 216–20.
40. Duff JH, Moffat J. Abdominal sepsis managed by leaving the abdomen open. *Surgery* 1981; **90**: 774–8.
41. Maetani S, Tobe T. Open peritoneal drainage as effective treatment of advanced peritonitis. *Surgery* 1981; **90**: 804–9.
42. Anderson ED, Mandelbaum DM, Ellison EC, Carey LC, Cooperman M. Open packing of the peritoneal cavity in generalized peritonitis. *Am J Surg* 1983; **145**: 131–5.
43. Bradley SJ, Jurkovich GJ, Pearlman NW, Stiegmann GV. Controlled open drainage of severe intra-abdominal sepsis. *Arch Surg* 1985; **120**: 629–31.
44. Mughal MM, Bancewicz J, Irving MH. 'Laparostomy': a technique for the management of intra-abdominal sepsis. *Br J Surg* 1986; **73**: 253–9.
45. Open management of the septic abdomen. Editorial. *Lancet* 1986; **ii**: 138–9.
46. Andrus C, Doering M, Herrmann VH, Kaminski DL. Planned reoperation for generalized intra-abdominal infection. *Am J Surg* 1986; **152**: 682–6.
47. Field TC, Pickleman J. Intra-abdominal abscess unassociated with prior operation. *Arch Surg* 1985; **120**: 821–4.
48. Dellinger EP, Wertz MJ, Meakins JL *et al.* Surgical infection stratification system for intra-abdominal infection. *Arch Surg* 1985; **120**: 21–9.
49. Krukowski ZH, Matheson NA. Emergency surgery for diverticular disease complicated by generalized and faecal peritonitis: a review. *Br J Surg* 1984; **71**: 921–7.
50. Elebute EA, Stoner HB. The grading of sepsis. *Br J Surg* 1983; **70**: 29–31.
51. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985; **13**: 818–28.

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Current spectrum of intestinal obstruction

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In a 12-month prospective study incorporating four neighbouring district general hospitals, 228 patients required a total of 236 admissions with intestinal obstruction. The aetiological factors included adhesions 75 (32 per cent), malignant disease 61 (26 per cent), strangulated hernias 59 (25 per cent), volvulus 10 (4 per cent), acquired megacolon 6 (3 per cent), pseudo-obstruction 4 (2 per cent), faecal impaction 6 (3 per cent) and miscellaneous 15 (6 per cent). The peak incidence for obstruction due to adhesions, malignant disease and strangulated hernias each occurred in the eighth decade. Surgery was performed within 48 h of admission in 29 per cent adhesive obstructions (22), 30 per cent obstructions due to malignant disease (18) and 68 per cent strangulated hernias (40) – bowel resection rates in these three groups were 13·5, 50 and 29 per cent, respectively. The overall mortality was 11·4 per cent (26 deaths) and postoperative mortality was 12·3 per cent (19 deaths). During the 12-month study period, 228 patients required a total of 2993 inpatient hospital days as a result of intestinal obstruction. Postoperative adhesions have become the commonest cause of intestinal obstruction but strangulated hernias and intra-abdominal malignant disease still account for 50 per cent of all cases and mortalities. Obstruction due to strangulated hernias and intra-abdominal malignant disease typically occurs in the elderly age group where a more aggressive policy of elective surgical intervention is likely to be associated with increased postoperative morbidity and mortality.

Keywords: Intestinal obstruction, morbidity, mortality, aetiology

Recent retrospective studies based on personal workload experiences suggest that there has been a considerable alteration in the pattern of intestinal obstruction encountered in western society over the past 50 years, but the spectra reported varied widely[1–5]. A 12-month prospective study incorporating four neighbouring district general hospitals, serving a total population of 591 000[6] was undertaken to determine if this trend was real or apparent and to provide an overview of the problem of intestinal obstruction as it exists in the UK today.

Patients and methods

All patients in whom a diagnosis of intestinal obstruction was established on admission to one of four neighbouring district general hospitals (Darlington Memorial, Bishop Auckland General, Hartlepool General and North Tees General) during the period 1 August 1985 to 31 July 1986 were included in the study. The diagnosis was that established by the surgical registrar based on the clinical picture, supported by radiological evidence (plain X-ray examination together with contrast studies, if indicated) and confirmed where appropriate at operation.

The provisional diagnosis of the referring general practitioner was noted and compared with the pre-operative diagnosis of the surgical registrar and the definitive diagnosis established at operation or, in the case of patients who were managed conservatively, established on the basis of the clinical picture and official interpretation of the X-ray findings by a consultant radiologist.

Surgery was defined as urgent (within 48 h of hospital admission) or delayed (at a later time during the same hospital admission). Operative details recorded included cause and site of the obstruction and nature of the operative procedure performed. Postoperative mortality was defined as death within 30 days of surgery while postoperative morbidity was defined in terms of duration of hospital stay.

Results

Aetiology

Two hundred and twenty-eight patients required a total of 236 admissions with intestinal obstruction during the study period, an incidence of 39·9 cases per 100 000 population per year: the causes are outlined in *Table 1*. Adhesions (32 per cent), malignant disease (26 per cent) and strangulated hernias (25 per cent) accounted for the vast majority of cases.

The previous operative procedures performed in patients with adhesive obstruction are outlined in *Table 2*. In 17 patients the nature of the previous surgery was unknown to the patient or had not been recorded. Five patients had undergone more than one previous operation.

Obstruction due to strangulated hernias occurred on 59 occasions in 57 patients (25 per cent). If patients under 10 years are excluded, strangulated hernias accounted for 20 per cent (45/220) of all adult obstructions. Hernia sites included 26 inguinal (21 right-sided), 21 femoral (15 right-sided), 6 incisional, 2 umbilical and 1 each obturator and Spigelian. Strangulated groin hernias occurred more frequently on the right side ($P < 0{\cdot}001$).

Obstruction due to intra-abdominal malignant disease occurred in 61 patients. Seventeen patients developed intestinal obstruction secondary to diffuse intra-abdominal malignant disease, eleven of whom had undergone previous bowel resection for tumour. No cases of small bowel obstruction due to primary tumour were recorded but secondary malignant disease caused localized small bowel obstruction in two patients – an extensive tumour of the gallbladder and grossly enlarged retroperitoneal lymph nodes secondary to testicular tumour spread. Obstruction due to primary colorectal cancer accounted for the remaining 42 cases (caecum 4, ascending

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Table 1 *Causes of intestinal obstruction*

Nature of obstruction	Number	Total (%)
Adhesions	75	32
Malignancy	61	26
Strangulated hernia	59	25
Volvulus	10	4
Acquired megacolon	6	3
Faecal impaction	6	3
Pseudo-obstruction	4	2
Gallstone ileus	3	1
Mesenteric infarction	3	1
Congenital band adhesions	3	1
Miscellaneous	6	3

Table 2 *Previous operations in adhesive obstruction*

Previous operations	Number
Appendicectomy	15
Colonic resection	15
Hysterectomy	7
Hysterectomy and salpingo-oöphorectomy	4
Salpingo-oöphorectomy	4
Cholecystectomy	3
Partial gastrectomy	2
Miscellaneous	10

colon 3, transverse colon 4, descending colon 5, rectosigmoid 26).

The sites for volvulus obstruction included sigmoid (7), caecum (2) and 1 midgut volvulus secondary to a Meckel's diverticulum attached anteriorly to the umbilicus. Three patients required six admissions because of acquired megacolon while pseudo-obstruction occurred in four elderly patients, two of whom were on long-term medication for psychiatric illnesses.

Age distribution

The patients ranged in age from 6 weeks to 90 years (mean age 69·6 years). The relatively large number of patients in the 0–10 age group (16), in which strangulated hernias accounted for 14 cases, was followed by a dramatic decline in incidence in the second decade of life and a steady increase thereafter to a peak incidence in the 71–80-year-old age group. The peak incidence for adhesions, hernias and malignant disease each occurred in the eighth decade (*Figure 1*).

Accuracy of pre-operative diagnosis

One hundred and sixty-nine of two hundred and thirty-six cases were referred by their general practitioners with a correct diagnosis of intestinal obstruction (72 per cent). Thirty-eight patients were diagnosed as having some other intra-abdominal pathology while no referral diagnosis was indicated in twenty-seven patients. A groin swelling had not been detected by the general practitioner in 17 of the 57 patients (30 per cent) with strangulated external hernias.

With the aid of radiological investigations and the benefit of continuous observation a correct diagnosis of intestinal obstruction was established by the surgical registrars in 95 per cent of cases (225/236). The site of the obstruction was correctly assessed as being small bowel, large bowel or both in 85 per cent of cases (201/236), but the presence of a strangulated groin hernia had not been identified before surgery in 6 patients (10 per cent).

Surgery

One hundred and fifty-four patients (66 per cent) underwent surgery during the same hospital admission. Strangulated hernias in the 0–10-year-old age group tended to reduce spontaneously in response to conservative management – only 3 of 14 presentations required urgent surgery and none required bowel resection. All but 2 of 39 adult patients in whom a strangulated hernia had been detected pre-operatively underwent surgery within 24 h of admission to hospital and the bowel resection rate in this group was 27 per cent (10/37) – one patient died within 1 h of admission owing to a perforated strangulated femoral hernia while elective re-admission was arranged for a second patient whose strangulated inguinal hernia reduced spontaneously (*Table 3*).

Urgent surgery (within 48 h) was performed in 29 per cent of adhesive obstructions (22/75) and 30 per cent of obstructions due to malignant disease (18/61), and bowel resection rates in the two groups were 14 per cent (3/22) and 44 per cent (8/18), respectively. The operative procedures performed in the 42 cases of obstruction due to colorectal cancer included right hemicolectomy, 7; transverse colectomy, 4; transverse defunctioning loop colostomy, 14; and Hartmann's resection, 17. Fifty per cent of adhesive obstructions (38/75) responded to conservative treatment alone and of the 12 patients with intra-abdominal malignant disease who did not undergo surgery 11

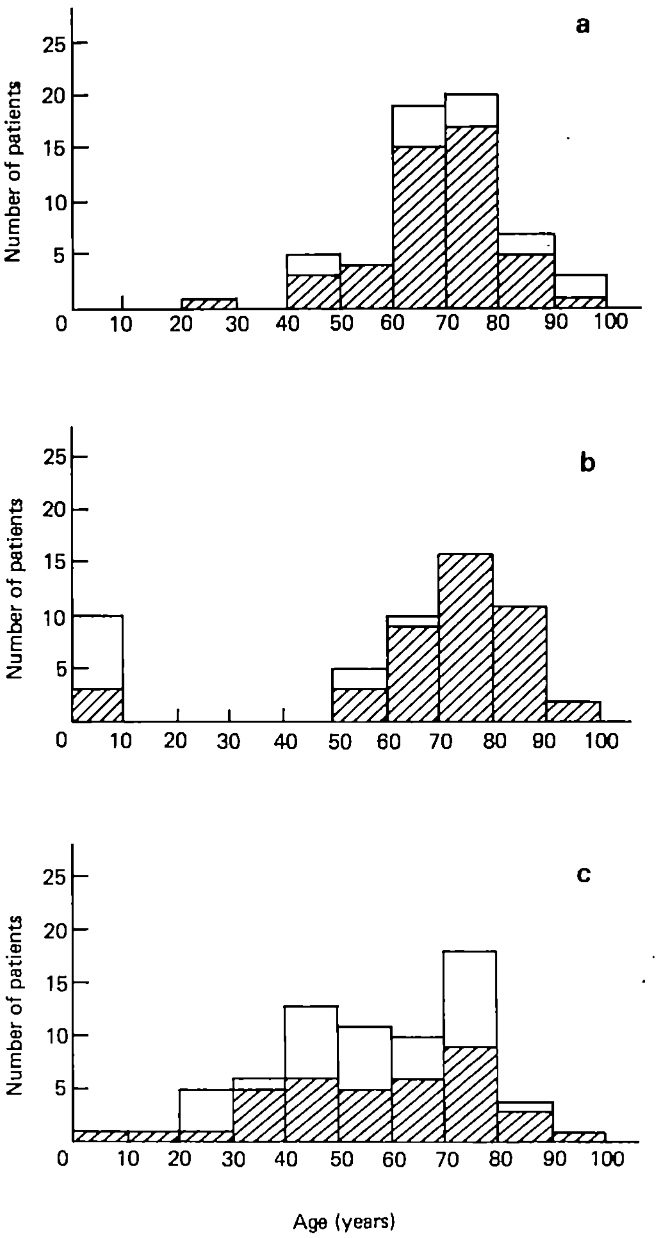

Figure 1 *Age distribution for common causes of intestinal obstruction:* **a**, *malignancy;* **b**, *hernia;* **c**, *adhesions;* ■, *operation group;* □, *no-operation group*

were known to have widespread metastatic disease, and 1 patient refused surgery.

Non-operative decompression was performed in two patients presenting with sigmoid volvulus – all seven remaining cases underwent primary bowel resection within 48 h of admission. Two of the three patients presenting with acquired megacolon ultimately underwent elective colonic resection while two of the four patients with pseudo-obstruction were treated conservatively by sigmoidoscopic decompression and two underwent defunctioning colostomy.

Mortality

Twenty-six patients died during the same hospital admission or within 30 days of operation – an overall mortality of 11·4 per cent. Postoperative mortality was 12·3 per cent (19/154) and included 7 patients with extensive disease thought to be incompatible with survival for whom no definitive procedure was performed (disseminated intra-abdominal malignancy, 5, extensive bowel infarction, 2). Mortality following definitive surgery was 8·2 per cent (12/147) and details are outlined in *Table 4*. All deaths due to intra-abdominal sepsis occurred in patients in whom the bowel had perforated proximal to the obstruction. All four deaths due to pulmonary embolism occurred in elderly patients (mean age 75·5 years, range 62–92 years) two of whom had underlying carcinoma.

Surgery was withheld in four patients known to have terminal diffuse intra-abdominal malignant disease while three patients died before surgical intervention – a 69-year-old woman with a perforated strangulated femoral hernia, an 80-year-old man with superior mesenteric artery embolism and a 77-year-old man with colonic obstruction of unknown aetiology and severe bilateral bronchopneumonia.

Morbidity

During the 12-month period, 228 patients spent a total of 2993 days in hospital due to intestinal obstruction. Mean hospital stay for patients with obstruction due to adhesions, hernias or intra-abdominal malignant disease, who required bowel resection was 15·4 days (range 9–39), 14·5 days (range 4–31) and 16·8 days (range 7–39), respectively, compared with 16·9 days (range 8–34), 11·6 days (range 3–30) and 17·9 days (range 8–31) for those in whom adhesiolysis, herniorrhaphy and proximal defunctioning colostomy, respectively, were performed.

Discussion

A continuous increase in the number of major abdominal operations[7,8] together with earlier detection and elective treatment of groin hernias and intra-abdominal malignant disease[2,3,7–9] has resulted in a considerable alteration in the spectrum of intestinal obstruction encountered in western society over the past 50 years (*Table 5*). In a retrospective study of 6982 patients admitted to 21 hospitals in Britain during the period 1925–30, strangulated hernias accounted for half the total cases while malignant disease was responsible for 13 per cent and adhesions accounted for a mere 7 per cent[10]. In a similar study from the USA two decades later (1942–45), the pattern had changed dramatically with adhesions now accounting for 31 per cent, malignant disease 27 per cent, and strangulated hernias only 10 per cent[11]. In the past two decades, however, the spectrum of intestinal obstruction in Britain, as reported in a number of retrospective series, varied widely[1–3] and the aim of this large prospective study was to provide a detailed account of the spectrum as it exists today. It confirms that adhesions have become the commonest single cause, but it also demonstrates that a surprisingly large proportion of intestinal obstructions still occur due to strangulated hernias and colorectal cancer, and these two conditions could hardly be considered to 'now play a relatively insignificant role' in the problem of intestinal obstruction as has recently been suggested[3].

Table 3 *Treatment and outcome in obstruction due to hernias, adhesions and malignant disease*

Cause	Surgical intervention		Bowel resection	Mortality
Hernia	No	2	—	1
	Within 48 h	37	10	2
	Delayed	6	3	1
Adhesions	No	38	—	0
	Within 48 h	22	3	1
	Delayed	15	2	0
Intra-abdominal malignancy	No	12	—	4
	Within 48 h	18	8	3
	Delayed	31	15	7

Table 4 *Mortality following definitive surgery for intestinal obstruction*

Patient no.	Sex	Age	Pathology	Procedure	Cause of death
1.	M	73	Carcinoma sigmoid colon	Hartmann's resection	Pulmonary embolus (7 days)
2.	M	66	Perforated carcinoma transverse colon	Extended right hemicolectomy	Intra-abdominal sepsis (3 days)
3.	M	62	Carcinoma descending colon	Hartmann's resection	Pulmonary embolus (30 days)
4.	F	79	Carcinoma sigmoid colon	Loop colostomy	Cardio-respiratory failure (5 days)
5.	F	92	Strangulated femoral hernia	Herniorrhaphy	Bronchopneumonia (12 days)
6.	F	81	Strangulated perforated femoral hernia	Small bowel resection; herniorrhaphy	Intra-abdominal sepsis (11 days)
7.	F	92	Strangulated incisional hernia	Ileum and transverse colon resected	Pulmonary embolus (17 days)
8.	F	84	Acquired megacolon	Colostomy + ileorectal anastomosis	Myocardial infarction (9 days)
9.	F	61	Adhesive obstruction; perforation; recent radiotherapy	Small bowel resection; adhesiotomy	Intra-abdominal sepsis (9 days)
10.	M	83	Volvulus sigmoid colon	Hartmann's resection	Chronic obstructive airways disease; ischaemic colostomy (3 days)
11.	M	73	Stenosed colostomy perforation	Tube colostomy	Intra-abdominal sepsis (1 day)
12.	M	75	Fibrous stricture rectum	Loop colostomy	Pulmonary embolus (6 days)

Table 5 *Patterns of intestinal obstruction over this century*

Study	Causes of obstruction (%) Adhesions	Hernia	Malignancy	Total cases	Mortality
Vick, 1925–30	7	49	13	6892	26
Wangensteen, 1942–52	31	10	27	1252	11
Ellis, 1962–83	31	23	30	279	8
Bevan, 1960–75	16	19	29	414	—
Bevan, 1976–80	38	13	17	277	—
McEntee *et al.* 1985–86	32	25	26	236	11

Many of the patients who presented with obstruction due to strangulated hernias and malignant disease were elderly (peak age group 71–80 years) and were suffering from other incapacitating illnesses. Such patients are less likely to seek medical advice for a groin swelling or disturbance in bowel habit and even if they were to do so, it is quite likely that many of them would be considered too elderly and frail for detailed investigation and elective operative intervention. This study was not designed to determine if these patients had previously sought medical advice for the condition that was eventually to cause intestinal obstruction, but the age distribution suggests that if the incidence of obstruction due to external hernias or malignant disease is to be further reduced, a more aggressive policy aimed at earlier detection and elective operative intervention is indicated particularly in elderly patients.

Apart from the high incidence of obstruction due to strangulated hernias and malignant disease, the series is also notable for the very low incidence of obstruction due to diverticular disease (one patient), which accounted for 3–5 per cent of all obstructions in the UK two decades ago[1–3]. This change probably reflects a greater overall awareness of the benefits of regular intake of bran and other high-fibre dietary products.

The pattern of operative intervention in this study (*Table 3*) may be interpreted as being indicative of the current approach to management of patients admitted to this region with intestinal obstruction. It is well recognized that the majority of strangulated hernias in children will reduce in response to conservative measures[13] and this policy was successful in 79 per cent of cases in this series. In contrast, urgent surgery was always performed in adult patients with obstruction associated with a recognized irreducible external hernia. Failure to identify an irreducible hernia resulted in delayed operative intervention in six patients with a 50 per cent bowel resection rate and was directly responsible for one mortality. The results would support a policy of conservative management for a minimum of 48 h in patients in whom signs of strangulation were absent and in whom the bowel obstruction is thought to be due to adhesions[5] and would refute the suggestion that all cases of mechanical small bowel obstruction require early operative intervention[14,15] – approximately 50 per cent of adhesive obstructions in this series responded to conservative management, while delayed operative intervention in those patients who failed to respond did not result in an increased bowel resection rate or increased mortality. Likewise, the majority of cases of obstruction due to intra-abdominal malignant disease (70 per cent) did not undergo urgent surgical intervention. In some, the presence of disseminated metastatic disease was clinically obvious (20 per cent), while in the remainder, presumably, the obstruction was incomplete or the ileocaecal valve was incompetent, obviating the need for urgent operative intervention and enabling both an accurate diagnosis to be established pre-operatively[16,17] and optimum rehydration, correction of electrolyte imbalance and nasogastric decompression to be carried out prior to surgical intervention.

Postoperative mortality following definite surgery was 8·2 per cent, which compares favourably with other recent series[1,5]. All deaths due to intra-abdominal sepsis[4] occurred as a result of perforation proximal to the obstruction and may have been prevented by earlier patient presentation to hospital, or earlier operative intervention. The four patients who died due to pulmonary embolism were elderly and immobile and two had underlying malignant disease. None had received prophylactic anticoagulants but, in retrospect, these patients constituted a high-risk group and perhaps a policy of anticoagulant prophylaxis[18,19] should be considered in elderly patients with intestinal obstruction of unknown aetiology about to undergo surgery.

Is the spectrum likely to change significantly in the years ahead? A more aggressive policy aimed at earlier detection and elective treatment of both groin hernias and large bowel cancer in elderly patients is likely to reduce further the already declining incidence of intestinal obstruction[2,3] but at an increased risk of postoperative morbidity and mortality because of the age group involved. With increasing numbers of major elective abdominal operations, it is also likely that, despite a greater understanding of the aetiology of adhesion formation[20], the problem of adhesive obstruction will assume even greater proportions.

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References

1. Nelson TW, Ellis H. The spectrum of intestinal obstruction today. *B J Clin Pract* 1984; **38**: 249–51.
2. Bevan PG. Adhesive obstruction. *Ann R Coll Surg Engl* 1984; **66**: 164–9.
3. Bevan PG. Acute intestinal obstruction in the adult. *Br J Hosp Med* 1982; 258–65.
4. Zadeh BJ, Davis JM, Canizaro PC. Small bowel obstruction in the elderly. *Am Surg* 1985; **51**: 470–3.
5. Bizer LS, Liebling RW, Delany HM, Gliedman ML. Small bowel obstruction. The role of non-operative treatment in simple intestinal obstruction and predictive criteria for strangulation obstruction. *Surgery* 1981; **89**: 407–13.
6. 1995 Planning Population by District for District Acute Specialties as in Regional Statistics Plan.
7. Quill DS, Devlin HB, Plant JA, Denham KR, McNay RA, Morris D. Surgical operation rates—a 12-year experience in Stockton-on-Tees. *Ann R Coll Surg Engl* 1983; **65**: 248–53.
8. Ellis H. Review of general surgery 1978. *Postgrad Med J* 1979; **55**: 223–40.
9. Vellacott KD, Smith JHF, Mortensen NJMcC. Rising detection rate of symptomatic Dukes' A colorectal cancers. *Br J Surg* 1987; 74: 18–21.
10. Vick RJ. Statistics of acute intestinal obstruction. *Br Med J* 1932; **2**: 546–7.
11. Wangensteen OH. *Intestinal Obstruction*. 3rd ed. Springfield: M. Thomas 1955.

12. Andrews NJ. Presentation and outcome of strangulated external hernias in a district general hospital. *Br J Surg* 1981; **68**: 329–32.
13. Palmer BV. Incarcerated inguinal hernias in children. *Ann R Coll Surg Engl* 1978; **60**: 121–4.
14. Shatila AH, Chamberlain BE, Webb WR. Current status of diagnosis and management of strangulation obstruction of the small intestine. *Am J Surg* 1976; **132**: 299–303.
15. Zollinger RM, Kinsey DL. Diagnosis and management of intestinal obstruction. *Am Surg* 1964; **30**: 1–5.
16. Koruth NM, Koruth A, Matheson NA. The place of contrast enema in the management of large bowel obstruction. *J R Coll Surg Edinb* 1985; **30**: 258–60.
17. Dudley HAF, Paterson-Brown S. Pseudo-obstruction. *Br Med J* 1986; **292**: 1157–8.
18. Kakkar VV, Corrigan TP, Fossard DP *et al.* Prevention of fatal postoperative pulmonary embolism by low doses of heparin: an international multicentre trial. *Lancet* 1975; **ii**: 45–51.
19. Segar S, Massey J, Sanderson JM. Low dose heparin prophylaxis against fatal pulmonary embolism. *Br Med J* 1975; **4**: 257–9.
20. Ellis H. The causes and prevention of intestinal adhesions. *Br J Surg* 1982; **69**: 241–3.

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Announcement

Multiple publication

In its instructions to authors *The British Journal of Surgery* states unequivocally that 'acceptance of original material is on the understanding that contributions are to this journal only . . .'. In the July edition the Journal carried an article by Ono and colleagues (Ono J, Katsuki T, Kodama Y, *Br J Surg* 1987; **74**: 607–9) describing a new approach in the management of oesophageal varices. This article based on 16 patients was accepted in good faith by the Editors on 4 March 1987. We were greatly distressed to see an article by the same three authors in the newly arrived May issue of *Surgery* (Ono J, Katsuki T, Kodama Y, *Surgery* 1987; **101**: 535–43) describing exactly the same technique and its use in what are unquestionably the same 16 patients. This article was accepted by *Surgery* in October 1986. The only difference between the articles lies in the more profuse illustration and the inclusion of a group not undergoing added splenopneumopexy in the *Surgery* version. However, the main purpose of the articles, namely description of the new technique, is achieved by almost identical means in the two publications.

It appears to us that this is another flagrant example in the long and sorry list of attempts at multiple publication of a given piece of work in different scientific journals. Our most charitable interpretation is that the authors have either not read or have not understood our clearly stated instructions. We have no wish to publish material already accepted by any journal and have no doubt that this view is shared by the Editors of *Surgery* and indeed by all of our fellow editors. It goes without saying that the Journal regrets this incident which has arisen due to circumstances beyond our control. We trust that this announcement will go some way to set the record straight.

The Editors

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Small bowel obstruction: computer-assisted prediction of strangulation at presentation

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A multivariate computer analysis has been performed on the presenting data of patients with simple small bowel obstruction that settled with conservative treatment (n = *120*) *and of patients with viable strangulation small bowel obstruction* (n = *38*) *and non-viable strangulation small bowel obstruction* (n = *39*) *found at operation. Initially only 66 per cent of patients with viable strangulation and 46 per cent of those with non-viable strangulation had been treated by immediate surgery after resuscitation. The remainder had been treated conservatively for a median of 3·8 and 2·2 days respectively before undergoing surgery. The computer predicted on the basis of presenting symptoms and signs that 82 per cent of patients with viable strangulation and 97 per cent of those with non-viable strangulation had or would develop strangulation and should have undergone immediate surgery. We advocate that the computer can assist in the management of patients with small bowel obstruction.*

Keywords: Small bowel obstruction, strangulation, computer diagnosis

Delayed surgical treatment of patients in whom small bowel obstruction is associated with strangulation carries a high mortality[1]. The ability to predict on admission those patients who have or will develop strangulation should lead to earlier treatment and reduced mortality. The difficulty in this prediction has led some to advocate immediate surgery in all cases of small bowel obstruction[2,3], but this exposes many patients who would have settled with conservative management to the risks of surgery. The decision regarding treatment is thus often a balance between the possibility of strangulation against the hazards of surgery.

Univariate analysis of signs and symptoms is not effective in predicting strangulation as no single factor can be used as a reliable means of differentiation[4]. It has been suggested that reliance can be placed on specific combinations of factors[5], although this has been disputed in a small prospective trial[6].

We report a study to develop a multivariate analysis system to predict at presentation which of the patients with small bowel obstruction have strangulation or will develop it during non-operative management.

Patients and methods

A retrospective analysis was made of the medical records of all patients admitted with small bowel obstruction to a hospital serving a population of 300 000 during the 12-year period 1973–1984. Patients in whom the combination of history, physical examination and radiographic findings were compatible with a diagnosis of mechanical small bowel obstruction or in whom the diagnosis was made at operation or autopsy were included. Patients with obstruction due to external herniae, adynamic ileus or mesenteric vascular insufficiency were not included. There remained 313 patients for initial study.

The type of obstruction was classified as:

Simple (*n* = 236), where there was no impairment to the blood supply of the bowel at operation or patients in whom the obstruction settled without operative intervention.

Viable strangulation (*n* = 38), where there was impairment to the blood supply but the bowel was judged to be viable following release of the obstruction.

Non-viable strangulation (*n* = 39), where there was impairment to the blood supply and following release of the obstruction the bowel was judged to be non-viable.

Of the 235 patients with simple small bowel obstruction 116 (49 per cent) underwent immediate or delayed surgery. There was no evidence of strangulation of the bowel at operation in these patients. However, these patients were excluded from further study since strangulation may subsequently have occurred had they not undergone surgery.

The patients in whom the simple small bowel obstruction settled with non-operative management (*n* = 120), those with viable (*n* = 38) and non-viable strangulation (*n* = 39) who either underwent immediate (within 6 h of admission) or delayed surgical treatment were studied (*Table 1*).

A multivariate analysis was performed on an IBM 3081 computer using SPSS statistical package. The following data which were obtained on admission were analysed: age, sex, duration of symptoms before admission, presence of pain (absent/intermittent/continuous), vomiting, abdominal distension, abdominal tenderness, peritonism, bowel sounds (increased/normal/reduced/absent), temperature, abdominal mass, heart rate, and white cell count.

In the initial analysis, data from patients with simple obstruction which settled with conservative treatment and data from patients with strangulation treated with immediate surgery were analysed in an attempt to discriminate between the three types of obstruction. Data were used in the form in which they were collected, e.g. heart rate in beats/min, and absence or presence of a symptom or sign indicated by 0 or 1 respectively. This analysis indicated that improvement could be achieved by replacing such a non-homogeneous mixture of discrete and continuous variables (mean values *Table 2*) with a uniform set of new discrete variables. The new discrete variables were calculated from the original continuous variables using suitable thresholds derived from the mean values in *Table 2*, and the features traditionally considered to be indicative of strangulation obstruction[7,8]. These features included the presence of continuous pain, peritonism, presence of an abdominal

Table 1 *Details of patients*

		Treatment		
	Number	Conservative	Immediate surgery	Delayed surgery
Simple	120	120	—	—
Viable strangulation	38	—	25 (1)	13
Non-viable strangulation	39	—	18 (3)	21 (3)

Mortality is given in parentheses

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Table 2 *Mean values of original variables*

	Simple	Viable	Non-viable
Age (years)	60·5	54·4	63·3
Sex (0=m, 1=f)	0·39	0·68	0·52
Duration (hours)	38	12	24
Pain (0=absent, 1=colic, 2=continuous)	1·17	1·36	1·6
Vomiting (0=absent, 1=present)	0·87	0·92	0·91
Distension (0=absent, 1=present)	0·68	0·73	0·80
Tenderness (0=absent, 1=present)	0·76	1·00	0·94
Peritonism (0=absent, 1=present)	0·12	0·52	0·75
Bowel sounds (1=increased, 2=normal, 3=reduced, 4=absent)	1·39	2·13	2·75
Mass (0=absent, 1=present)	0·02	0·18	0·22
Temperature (°C)	36·9	36·7	36·8
Heart rate (beats/min)	89	85	100
White cell count ($\times 10^9$/l)	10·9	13·1	12·7

Table 3 *Thresholds used in deriving new variables*

Age (years)	60
Duration (hours)	20
Pain (0=absent, 1=colic, 2=continuous)	1
Bowel sounds (1=increased, 2=normal, 3=decreased, 4=absent)	2
Temperature (°C)	36·5–37·3
Heart rate (beats/min)	90
White cell count ($\times 10^9$/l)	11

Table 4 *Classification of patients by multivariate analysis compared with actual diagnostic groups*

Actual diagnosis		Computer analysis		
Classification	Total	Simple	Viable	Non-viable
Simple	120	102 (85%)	15 (13%)	3 (2%)
Viable	38	7 (18%)	23 (61%)	8 (21%)
Non-viable	39	1 (3%)	9 (23%)	29 (74%)

mass, reduced or absent bowel sounds, tachycardia, pyrexia or hypothermia and leucocytosis. Simple thresholds were used with the exception of body temperature which had a normal range defined as 36·5–37·3°C with an abnormal range outside these values. The thresholds in deriving the new variables are shown in *Table 3*. The program derived was then used to categorize all patients into the three types of obstruction, including those patients who had initially been treated conservatively and in whom strangulation was subsequently found at operation.

Results

Initially 34 per cent of patients with viable strangulation found at operation had been treated conservatively within hospital for a median 3·8 days before surgery, and 54 per cent of patients with non-viable strangulation and been treated conservatively for a median 2·2 days before surgery. There was one death among the 38 patients (3 per cent) with viable strangulation obstruction, whereas 6 (15 per cent) of the 39 patients with non-viable strangulation died.

The results of discriminant analysis using the discrete values are given in *Table 4*, which shows the classifications given by the computer to cases from the three categories of obstruction. The computer correctly diagnosed 85 per cent of cases of simple obstruction, and allocated 82 per cent of patients with viable and 97 per cent with non-viable strangulation to the strangulation categories.

Discussion

Small bowel obstruction is usually divided into two categories: simple and strangulated. Some authors define strangulated as implying haemorrhagic infarction (i.e. non-viability)[9,10], whereas others include any case in which there is impairment of the blood supply[4,11]. It is difficult to compare studies. We have divided small bowel obstruction into simple, viable strangulation and non-viable strangulation as suggested by Sarr *et al.*[6]. The decision between the latter two was dependent on the opinion of the surgeon at the time of surgery as to whether the bowel was viable. It is recognized though that this decision is not always accurate, but no patient developed gangrenous bowel who had been judged to have viable strangulation at operation.

The mortality of 15 per cent in patients judged to have non-viable bowel and requiring a resection is similar to that in other studies[4,6,8,11,12]. A prospective study[6] found that 'senior surgeons' failed to diagnose correctly 50 per cent of cases of small bowel obstruction as having strangulation pre-operatively and in retrospective studies 50–85 per cent of patients are diagnosed incorrectly at presentation[4,11,13]. In our study over half the patients with non-viable strangulation had been treated conservatively for more than 2 days before undergoing surgery. If these patients had been operated upon soon after admission it is possible that in some the bowel would have been viable, resection unnecessary and the mortality reduced to that of patients with viable strangulation (4 per cent). It is important that such patients be identified on admission. The alternative is to operate on all patients with mechanical small bowel obstruction after suitable fluid and electrolyte replacement. But since 120 patients with simple small bowel obstruction settled following conservative treatment it would expose this group to the morbidity and mortality associated with surgery, without guaranteeing a prevention of future episodes of small bowel obstruction in many cases.

The presence of certain features ('classical factors') has traditionally been used to predict the presence of ischaemia. Analysis of individual factors has shown that no single one can be used as a reliable method of predicting strangulation[4,14]. It has been suggested that specific combinations of factors could be used to predict ischaemia[5,7]. Stewardson *et al.*[5] found that 90 per cent of patients with gangrenous bowel had at least two of the following: fever, leucocytosis, tachycardia and localized abdominal tenderness, and all patients had at least one. But both Bizer *et al.*[8] and Sarr *et al.*[6] have each described patients with strangulation obstruction who had none of the defined classical factors. Some of the factors that we studied are very subjective, for instance bowel sounds. We found that the clinicians' description of bowel sounds fell into four categories, and we included these data in the analysis. The computer, by using its derived thresholds, was able to simplify the situation by categorizing bowel sounds into two types.

We used a program developed from the data at presentation of patients with simple obstruction that settled with conservative treatment and of patients with strangulation treated with immediate surgery. The computer therefore 'learnt' from some of the patients. The program derived was then applied to the data of all patients including those in whom strangulation was found after a period of conservative treatment. The computer identified correctly 85 per cent of patients with simple obstruction, 61 per cent with viable strangulation and 74 per cent with non-viable strangulation. More importantly it allocated correctly 82 per cent of those with viable strangulation and 97 per cent of those with non-viable strangulation to categories in which strangulation was present or would occur. These patients should have undergone immediate surgery after resuscitation. This contrasts with the diagnostic accuracy of the surgeon since only 66 per cent of patients with viable strangulation and 46 per cent of patients with non-viable strangulation were diagnosed by the surgeon as requiring immediate surgery.

We do not advocate that the decision to operate or not should be made by the computer, but that the computer may assist in those cases which the surgeon initially decides to treat conservatively. This may reduce the number of patients who are subsequently found to have strangulation after a period of non-operative treatment. We are currently performing a prospective evaluation of this computer program.

References

1. Playforth RH, Holloway JB, Griffin WO. Mechanical small bowel obstruction: a plea for earlier surgical intervention. *Ann Surg* 1970; **171**: 783–8.
2. Davidson AT. Early operation in the treatment of small bowel obstruction. *J Nat Med Assoc* 1981; **73**: 245–6.
3. Ellis H. Mechanical intestinal obstruction. *Br Med J* 1981; **283**: 1203–4.
4. Silen W, Hein MF, Goldman L. Strangulation obstruction of the small intestine. *Arch Surg* 1962; **85**: 137–45.
5. Stewardson RH, Bombeck T, Nyhus LM. Critical operative management of small bowel obstruction. *Ann Surg* 1978; **187**: 189–93.
6. Sarr MG, Bulkley GB, Zuidema GD. Pre-operative recognition of intestinal strangulation obstruction. *Am J Surg* 1983; **145**: 176–82.
7. Leffal LD, Syphax B. Clinical aids in strangulation intestinal obstruction. *Am J Surg* 1970; **120**: 756–9.
8. Bizer LS, Liebling RW, Delany HM, Gliedman ML. Small bowel obstruction. *Surgery* 1981; **89**: 407–13.
9. Saltzstein EC, Marshall WJ, Freeark RJ. Gangrenous intestinal obstruction. *Surg Gynecol Obstet* 1962; **114**: 694–700.
10. Delany HM. Prognostic factors in infarction of the intestine. *Surg Gynecol Obstet* 1972; **135**: 253–6.
11. Shatila AH, Chamberlain BE, Webb WR. Current status of diagnosis and management of strangulation obstruction of the small bowel. *Am J Surg* 1976; **132**: 299–303.
12. Barnett WO, Petro AB, Williamson JW. A current appraisal of problems with gangrenous bowel. *Ann Surg* 1976; **183**: 653–9.
13. Davis SE, Sperling L. Obstruction of the small intestine. *Arch Surg* 1969; **99**: 424–6.
14. Zollinger RM, Kinsey DL. Diagnosis and management of intestinal obstruction. *Am J Surg* 1964; **30**: 1–5.

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Symptomatic submucosal lipoma of the large bowel

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Symptomatic large bowel lipomata may be of considerable size and usually present in middle age with symptoms of obstruction or bleeding. Although they are rare, their recognition is important so that patients may be spared unnecessary colonic resection for a presumptive malignant diagnosis. Colonoscopic removal may often be feasible. Six cases are reported together with a review of the literature emphasizing the characteristic features.

Keywords: Lipoma, colon, colonic neoplasms, colonic polyps, colonoscopy, rectal neoplasms

Lipomata may arise throughout the gastrointestinal tract. In the wall of the intestine most lie in the submucosal plane, less frequently they are found in the subserosal plane[1]. More than two-thirds are found in the large bowel[2] where lipomata are the commonest benign neoplasms after adenomata. Nevertheless they are uncommon. Lipomata of the large bowel are reported as incidental findings in 0·32–0·5 per cent of cases in large series of autopsies[3,4]. Symptomatic large bowel lipomata are rare, accounting for less than 0·002 per cent of surgical patients treated at the Mayo clinic over a 50-year period[4]. As a result of their rarity and variable presentation, they are usually mistaken for more serious pathology and consequently more radical surgery than is necessary is often performed.

Patients and methods

All patients with symptomatic lipomata of the large bowel presenting to the Leicester General Hospital and the Leicester Royal Infirmary in an 11-year period (1976–86 inclusive) were identified by a search of the computerized histopathology records. Incidental asymptomatic lesions were not included in this review.

Results

The search yielded five patients within this period. Their clinical features together with those of a sixth case, presenting before these dates, are reviewed. During this same time period 5 asymptomatic lipomata were identified and for comparison 3215 carcinomas of the colon and rectum were treated. The findings in the six cases of symptomatic lipomata are summarized in *Table 1*. Their ages ranged from 36 to 77 years with a mean of 52·7 years. Five of the six were women. Lipoma size varied from 3 to 6 cm with a mean of 5·2 cm.

Case 1

A 44-year-old woman presented as an emergency with a 1-week history of intermittent lower abdominal colic. Six months previously she had passed blood and mucus in her stool for 1 week, but this had resolved spontaneously. She was pyrexial and examination revealed diffuse lower abdominal tenderness. A presumptive diagnosis of acute diverticulitis was made and her symptoms settled with conservative treatment. A barium enema showed a large polypoid filling defect in the mid-transverse colon and a transverse colectomy was performed. The polyp had a maximum diameter of 6 cm and was ulcerated at its apex. Histology showed it to be a submucosal lipoma.

Case 2

A 76-year-old man presented as an emergency with a 2-day history of fresh rectal bleeding and a 6-week history of altered bowel habit with loose blood-stained motions. Colonoscopy revealed a large polypoid lesion in the descending colon which was thought to be fixed and malignant. Laparotomy showed a palpable lesion at the splenic flexure and left hemicolectomy was performed. A 3 cm diameter polyp was found within the bowel lumen. This was ulcerated at its apex and histology showed a submucosal lipoma.

Case 3

A 77-year-old woman complained of a 7-year history of intermittent lower abdominal pain and a 4-week history of passing fresh blood and mucus per rectum. Abdominal examination revealed fullness in the left iliac fossa. Barium enema showed a smooth polypoid lesion intussuscepting at the junction of the descending and sigmoid colon. The possibility of an intussuscepting lipomatous polyp was considered and, in view of her age, colonscopic snare removal was felt to be appropriate.

Unfortunately she presented as an emergency, before colonoscopy could be performed, with large bowel obstruction and colonic perforation. At laparotomy there was an intussuception of the splenic flexure and a local resection of this region was performed. Pathological examination of the specimen revealed a polyp, with a maximum diameter of 5·5 cm, acting as an intussusceptum. The polyp was ulcerated at its apex and histology showed it to be a submucosal lipoma.

Case 4

A 62-year-old woman was referred with a history of a single painless rectal bleed. Colonoscopy revealed a smooth polyp in the sigmoid colon. Colonoscopic polypectomy was performed. The polyp was 4·5 cm in diameter and smooth in appearance. On microscopy there was ulceration of the mucosa overlying a submucosal lipoma.

Case 5

A 35-year-old female patient presented as an emergency with lower abdominal pain associated with a prolapsed rectal polyp. There were no previous bowel symptoms. Examination confirmed a 6 cm diameter soft polyp arising from the lateral wall of the rectum, The stalk was ligated and the polyp excised. There were numerous areas of ulceration on its surface and histology showed a submucosal lipoma.

Case 6

A 51-year-old woman presented with a 3-week history of abdominal pain, vomiting and diarrhoea. She had passed approximately 250 ml of fresh blood per rectum on one occasion followed by mucus. Barium enema showed an intussusception at the mid-transverse colon and at this time an upper abdominal mass was palpable. At laparotomy a 6 cm pedunculated smooth polyp was found to be arising from the ascending colon and intussuscepting into the transverse colon. This was partially

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Table 1 *Summary of the six patients with symptomatic large bowel lipomata*

	Age (years)	Sex	Site	Size (cm)	Diagnosis	Treatment
Case 1	44	F	Transverse colon	6·0	Adenomatous polyp	Transverse colectomy
Case 2	76	M	Descending colon	3·0	Carcinoma	Left hemicolectomy
Case 3	77	F	Splenic flexure	5·5	Benign polyp ? lipoma	Local resection
Case 4	62	F	Sigmoid colon	4·5	Benign polyp	Endoscopic polypectomy
Case 5	36	F	Rectum	6·0	Rectal polyp ? benign	Local excision
Case 6	51	F	Ascending colon	6·0	Carcinoma	Right hemicolectomy

Table 2 *Previous reports of symptomatic large bowel lipomata*

	No. of cases	Sex		Mean age (years)	Site				
		Male	Female		Ascending	Transverse	Descending	Sigmoid	Rectum
Comfort, 1931 Own cases (Ref. 1)	3	1	2	45·3	1	1	0	1	0
Comfort, 1931 Review (Ref. 1)	26	13	13	47·6	12	6	3	2	3
Ryrberg, 1957 (Ref. 10)	4	0	4	62·5	3	1	0	0	0
Ginzburg, 1958 (Ref. 11)	10	5	5	—	4	3	1	2	0
Haller, 1964 (Ref. 11)	5	1	4	71·2	3	2	0	0	0
Mukamel, 1978 (Ref. 12)	2	0	2	57·0	1	0	0	1	0
Michowitz, 1985 (Ref. 8)	8	2	6	65·3	4	1	2	0	1
Present series	6	1	5	57·7	1	2	1	1	1
Combined data	64	23 (36%)	41 (64%)	54·9	29 (45%)	16 (25%)	7 (11%)	7 (11%)	5 (8%)

reduced and a right hemicolectomy was performed. Histology showed the polyp to be a submucosal lipoma.

Discussion

Brunner, in 1899[5], was one of the first authors to report a symptomatic submucosal lipoma of the large bowel. Since then several series of cases of large bowel lipoma have been published[1,3,6–8]. However these series all include lesions found incidentally, both at operations for other pathology and at necropsy and the number of reported incidental and asymptomatic cases far exceeds the symptomatic cases. In addition to his own patients, Comfort, in 1931[1], made a comprehensive review of all previously reported gastrointestinal lipomata which only included 29 symptomatic large bowel cases. One of the largest series of gastrointestinal lipomata, comprising 164 cases, was reported by Mayo[2], including 119 large bowel lesions. Of the total 164 cases 75 (46 per cent) were symptomatic but unfortunately it is not clear how many of these were large intestinal. This is also true of some other publications[4,6,7,9]. In only a few reports, therefore, is it possible to determine the clinical features associated with symptomatic patients alone. These are summarized in *Table 2*.

Site

In four of the six patients the lesions were in the left colon or rectum. However, from the combined data of the 64 patients shown in *Table 2*, the commonest site for symptomatic solitary large bowel lipoma is the ascending colon (including caecum), followed by the transverse colon (including both hepatic and splenic flexures), descending colon, sigmoid colon and rectum. This decreasing incidence passing distally has been observed previously[3,7,8]. All six of our lesions were submucosal and we did not encounter a single case of the less common subserosal type. None of the six patients concerned had multiple lipomata although multiple lesions are reported in up to 24 per cent of cases[7].

Age and sex

The mean age of our patients (57·7 years) is similar to the combined data mean age of 54·9 years. Others have reported that the peak incidence for lipomata of the large bowel is in the sixth decade[7]. This may be related to the slow rate of growth of these benign tumours which often do not present till they are large[3,8]. Consequently, they present at an age when there is a high incidence of colorectal carcinoma[4].

Although five of our six patients were women and the combined data for symptomatic lipomata (*Table 2*) shows a female predominance (1·8:1) the literature disagrees on this point. Some authors have reported a female predominance[3,7,8,11], while others found a nearly equal sex incidence[4,10]. This may reflect bias due to different hospital populations.

Clinical presentation

Since the number of large bowel lipomata found incidentally at necropsy or operation far exceeds the number of surgically treated cases[3,7], it must be assumed that most lesions cause no symptoms at all. In symptomatic cases the clinical features relate to the size of the lesions. Large lipomata may cause obstructive symptoms and may also initiate intussusception. The mucosa overlying a large lipoma may be atrophic and may also be traumatized resulting in ulceration and bleeding which can be profuse[13]. Because of their soft consistency, there is usually no mass to feel on abdominal examination. The vague mass palpable in two of the above cases (cases 3 and 6) was almost certainly intussuscepted bowel or faecal masses proximal to the intussusception. Rectal lipomata may be palpable on digital examination of the rectum but these represent a small proportion of the symptomatic cases.

Investigations

Only a minority (up to 20 per cent) of large bowel lipomata can be seen using the rigid sigmoidoscope. They can, however, be visualized by colonoscopy and barium enema examination. The colonoscopic appearances are very similar to those of adenomatous polyps but can resemble carcinoma when the overlying mucosa is ulcerated. Biopsy produces benign tissue but this is not recommended for polypoid lesions. Adipose tissue lying beneath normal or ulcerated mucosa is likely to be non-diagnostic and, if a polyp proves to be an adenoma, biopsy does not exclude malignancy, the risk of malignancy increasing with the size of the polyp[14] and the age of the patient[15]. The diagnosis is therefore usually made histologically after the lesion has been excised often together with a wide margin of normal large bowel.

Several radiographic features of lipomatous polyps on barium enema examination have been reported. These are of considerable importance if the diagnosis is to be made pre-operatively and the patient spared unnecessary general anaesthesia and colonic resection. A submucosal lipoma is a smooth filling defect which may have a lobulated appearance. Because it is covered with normal mucosa, its outline is often sharper than that of an adenomatous polyp, with less barium coating. Ulceration of the mucosa, however, may make this difference less obvious. The high fat content of the lipoma results in greater radiolucency than is exhibited by adenomatous polyps on contrast radiography and the use of a water enema to enhance this differential absorption has been advocated[16]. Because they are soft in consistency, external pressure or peristalsis may result in deformation which has been termed the 'squeeze sign'[6]. This may be the most useful sign since it distinguishes lipomas from other types of colonic polyp which are all firmer in consistency. Demonstration of this sign, however, requires suspicion of the diagnosis at the time of barium enema so that the necessary additional manoeuvres can be performed.

Treatment and prognosis

Because of their location and the age of the patients at presentation, large bowel lipomata are usually treated on the basis of a presumptive malignant diagnosis. This results in general anaesthesia and colonic resection with its attendant mortality and morbidity. With the advent of colonoscopy and diathermy snare polypectomy[17] operative intervention can be avoided in many cases (as in Case 4). In expert hands, large pedunculated and even large sessile lesions can be removed endoscopically[18]. Caution must however be exercised in the case of broad-based lesions since snare removal carries increased risk of bleeding and perforation. Use of snare removal requires awareness of the characteristic features of colonic lipomas and strenuous efforts to demonstrate them radiologically.

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References

1. Comfort MW. Submucous lipomata of the gastro-intestinal tract: report of twenty-eight cases. *Surg Gynecol Obstet* 1930; **52**: 101–18.
2. Mayo CW, Pagtalunan RJG, Brown DJ. Lipoma of the alimentary tract. *Surgery* 1963; **53**: 598–603.
3. Haller JD, Roberts TW. Lipomas of the colon: a clinicopathologic study of 20 cases. *Surgery* 1964; **55**: 773–81.
4. Long GC, Dockery MB, Waugh JM. Lipoma of the colon. *Surg Clin N Am* 1949; **29**: 1233–43.
5. Brunner C. Ein beitrag zur chirurgie und pathologischen anatomie der darminvagination. *Beitr Klin Chir* 1899; **25**: 344–63.
6. Hurwitz MM, Redleaf PD, Williams HJ, Edwards JE. Lipomas of the gastrointestinal tract. An analysis of seventy-two tumours. *Am J Roentgenol* 1967; **99**: 84–9.
7. Castro EB, Stearns MW. Lipoma of the large intestine: a review of 45 cases. *Dis Col & Rect* 1972; **15**: 441–4.
8. Michowitz M, Lazebnik N, Noy S, Lazebnik R. Lipoma of the colon. A report of 22 cases. *Am Surg* 1985; **51**: 449–54.
9. Ackerman NB, Chughtai SQ. Symptomatic lipomas of the gastrointestinal tract. *Surg Gynecol Obstet* 1975; **141**: 565–8.
10. Ryrberg CH. Lipoma of the colon. Report of four cases and review of the literature. *Acta Chir Scand* 1957; **111**: 45–53.
11. Ginzburg L, Weingarten M, Fischer MG. Submucous lipoma of the colon. *Ann Surg* 1958; **148**: 767–72.
12. Mukamel E, Wollock Y, Glanz I, Dintsman M. Lipomas of the large intestine. *Am J Proct Gastroenterol Colon Rect Surg* 1978; **29**: 30–3.
13. Key JC, Roberts JW. Massive bleeding from colonic lipoma. *Arch Surg* 1980; **115**: 889–90.
14. Morson B. The polyp–cancer sequence in the large bowel. *Proc R Soc Med* 1974; **67**: 451–7.
15. Waye JD. Colon polyps: problems, promises, prospects. *Am J Gastroenterol* 1986; **81**: 101–3.
16. Margulis AR, Jovanovich A. The roentgen diagnosis of submucous lipomas of the colon. *Am J Roentgenol* 1960; **84**: 1114–20.
17. Williams CB, Hunt RH, Loose H, Riddell RH, Sakai Y, Swarbrick ET. Colonoscopy in the management of colon polyps. *Br J Surg* 1974; **61**: 673–82.
18. Christie JP. Colonoscopic excision of large sessile polyps. *Am J Gastroenterol* 1977; **67**: 430–8.

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Short note

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Elective repair of groin hernias in the elderly

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Elective repair of groin hernia is a simple and safe surgical procedure at any age, and is a well known example of the preventative value of early surgery[1]. Conversely, the overall risks of emergency surgery in the elderly, measured by morbidity and mortality, may increase two- or threefold[2]. Nevertheless, many elderly patients are still admitted to our hospital with symptomatic groin hernias. We have tried to establish the exact risk to the patients and the reasons why elective surgery is not preventing their emergency admissions.

Patients, methods and results

During 1984, 95 patients over the age of 65 years were admitted for inguinal hernia operations, 46 (48·4 per cent) as emergencies and 49 electively. The emergency group was significantly older, median age 76 years (range 65–88) compared with 70 years (range 65–88) for the elective group (χ^2 with Yates's correction factor $P < 0{\cdot}01$). The only death occurred in the emergency group. Elective patients stayed $9{\cdot}3 \pm 7{\cdot}3$ days (mean ± s.d.), but after emergency surgery this rose to $13{\cdot}2 \pm 8{\cdot}7$ days ($0{\cdot}05 > P > 0{\cdot}02$, Student's *t* test).

In this period, 18 elderly people were admitted because of femoral hernias: 16 as emergencies and 2 electively. Three emergency patients died, one on admission due to protracted bowel obstruction, and two postoperatively. Neither elective patient died.

To investigate where responsibility for these emergencies lay, we sent a postal questionnaire to the 48 survivors of emergency surgery and received 25 usable replies. Of these patients, 20 knew of their hernia before admission and most (18) for longer than 1 year. Only two patients had failed to tell their GPs, but in thirteen cases (including three patients who had femoral hernias) the GP chose not to refer for elective surgery. None of the five patients referred for surgical opinion was awaiting admission.

We then asked 406 senior physicians, GPs, geriatricians and surgeons in the West Midlands if they would advocate elective surgery for (i) a small painless reducible inguinal hernia in a 79-year-old man, (ii) an asymptomatic femoral hernia in a frail 80-year-old woman; 333 replied. Elective repair was seldom chosen for inguinal hernia (physicians 10·3 per cent, GPs 21 per cent, geriatricians 22·6 per cent, surgeons 29·3 per cent) and even for the more notorious femoral hernia, only 37·8 per cent of GPs advocated elective repair, compared with 48·7 per cent of physicians, 61·4 per cent of geriatricians and, to our surprise, only 77·7 per cent of surgeons.

Discussion

Elderly patients who require an emergency groin hernia repair and survive are likely to stay in hospital longer compared with equivalent elective patients. Reported mortality rates range from 9·7 to 61 per cent when resection of gangrenous bowel is required[3,4]. Thus our overall mortality rate of 6·5 per cent appears favourable but not compared with the zero mortality for elective surgery.

Most patients knew about their hernia before the acute event and, although many (90 per cent) had drawn their GP's attention to it, very few had been referred for elective surgery. With the development of local and regional anaesthesia virtually no patient need be refused elective surgery on medical grounds. Indeed, several of our surgical respondents specified that they prefer local anaesthesia, and there is evidence that local anaesthesia offers some postoperative advantages when compared with general anaesthesia (e.g. rapid mobilization[5], less respiratory compromise[6] and obviation of the need for urinary catheterization[7]).

Several respondents to the management questionnaire select candidates for inguinal hernia surgery depending upon whether the hernia is clinically direct or indirect. Unfortunately this is known to be inaccurate[8] and should not dictate management. According to our survey, some surgeons would not offer an elective repair to elderly patients with an asymptomatic inguinal hernia, and indirectly this attitude may prejudice the referral practice of non-surgeons.

We are concerned that several femoral hernias were not referred since the consensus of surgical opinion is strongly in favour of elective repair[9]. The vignette study results confirm this practice to be widespread since a mere 37·8 per cent of GPs would refer an elderly woman with a painless femoral hernia. Surprisingly, 22 per cent of surgeons would not offer elective repair.

One view of the efficiency of a health service is the extent to which it is capable of reducing preventable emergencies, of which groin hernia complications are a very good example[10]. A total of 1947 patients over 65 years of age died from the complications of such hernias during 1984 in England and Wales (unpublished data from the West Midlands Regional Health Computer Centre, office of statistics). Our study suggests that patients alert their doctors when they notice a hernia, but too often they fail to receive an elective repair. Sometimes this is the fault of the referring doctor and we believe all patients should be offered surgery. However we would speculate that, while so many patients with hernias languish on waiting lists, practitioners and surgeons are wrongly exercising a selective policy at the expense of the elderly.

References

1. Jesseph JE. In: Nyhus LM, Harkins HN, eds. *Hernia*. Philadelphia: Lippincott, 1964: 262.
2. Stahlgren L. An analysis of factors which influence mortality following extensive abdominal operation on geriatric patients. *Surg Gynaecol Obstet* 1961; **113**: 283–92.
3. Hjaltason E. Incarcerated hernia. *Acta Chir Scand* 1981; **147**: 263–7.
4. Tasker DG. Femoral hernia: a continuing source of avoidable mortality. *Br J Clin Pract* 1982; **36**: 141.
5. Teasdale C, McCrum A, Williams NB, Horton RE. A randomised controlled trial to compare local with general anaesthesia for short-stay inguinal hernia repair. *Ann R Coll Surg Engl* 1982; **64**: 238–42.
6. Godfrey PJ, Greenen J, Ranasinghe DD, Shabetary SM, Pollock AV. Ventilatory capacity after three methods of anaesthesia for inguinal hernia repair: a randomised, controlled clinical trial. *Br J Surg* 1981; **38**: 587–9.
7. Glassfow F. Inguinal hernia repair under local anaesthesia. *Ann R Coll Surg Engl* 1984; **66**: 382–7.
8. Ralphs DN, Brain AJJ, Grundy DJ, Hobsley M. How accurately can direct and indirect inguinal hernias be distinguished? *Br Med J* 1980; **280**: 1039.
9. Giles GR. In: Cuscheri A, Giles GR, Moossa AR, eds. *Essential Surgical Practice*. Bristol: John Wright and Sons, 1982: 881.
10. Ellis H. *Intestinal Obstruction*. New York: Appleton-Century-Crofts, 1982: 175.

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Surgical management of posterior pharyngeal pulsion diverticula: inversion versus one-stage excision

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At present one-stage excision of the posterior pharyngeal pulsion diverticulum is the most popular method of treatment in the UK and the USA. We have reviewed 53 patients who have presented to this unit between 1968 and 1986, to compare the results of different surgical techniques. Of these, 21 underwent excision and myotomy, 20 inversion and myotomy, and 9 myotomy alone. The results show that the mortality for the whole group was 4 per cent, but there were no deaths in either the inversion or myotomy group. The excision group had a complication rate of 52 per cent, compared with 30 per cent for inversion, and also had more major problems such as fistula. Median hospital stay was shorter for inversion than for excision, at 7 and 10 days respectively. In summary we believe that inversion of the posterior pharyngeal pulsion diverticula is now the surgical treatment of choice.

Keywords: Pharyngeal diseases, hypopharyngeal diseases, oesophageal diverticula

The posterior pharyngeal pulsion diverticulum was first described by Mr A. Ludlow[1], a surgeon of Bristol in 1764. The diverticulum arises posteriorly between the thyropharyngeus above and the cricopharyngeus below, at a weak area known as Killian's dehiscence. Mucosal herniation results in the formation of a blind ending sac which causes the symptom pattern of dysphagia, regurgitation and weight loss. It is an eminently curable condition but if it is left alone it may at worst kill the patient. However, surgery carries a small mortality and a considerable morbidity.

The first successful excision was carried out by Wheeler[2] in 1886, but subsequently one-stage excision fell into disrepute owing to the high mortality and morbidity as emphasized in Stetton's review[3] in which he reported an 18·7 per cent mortality and only a 42 per cent primary healing rate. Consequently other methods were developed including two-stage excision, endoscopic diathermy division of the diverticulo-oesophageal septum, diverticulopexy, and finally inversion or invagination of the diverticulum.

Inversion or invagination of the diverticulum was first described by Girard[4] in 1895, who successfully treated two patients with this technique. Halstead[5] used a similar method, closing the neck of the sac with a purse-string suture which he inserted while outlining the sac with a bougie. He believed that the method was only appropriate to small sacs. Bevan[6] modified the technique in 1917 in the Sippy–Bevan operation in which a series of purse-string sutures along the body of the sac were used to reduce the sac to a stump, in order to obliterate it. All three pioneers of this method were convinced that it reduced the risk of fistula and serious complications such as mediastinitis.

During this period Goldman[7] developed a two-stage procedure which involved bringing the sac out to the skin surface, creating a controlled fistula, allowing fibrosis to envelop the sac wall and later resecting the sac wall to allow closure of the fistula. The technique was popularized by Lahey[8], but since the advent of antibiotics one-stage excision has re-emerged as the treatment of choice in the UK and North America. However, it still carries a considerable mortality and morbidity.

Patients and methods

During the 20-year period between 1966 and 1986, 64 patients with posterior pharyngeal pulsion diverticula have been treated at this unit. Of these, 11 patients either refused surgery, or were relatively asymptomatic and in poor general health such that they were advised against surgery; this group had a mean age of 68·4 years at presentation. A total of 53 patients underwent surgery for their diverticula, the majority by excision, inversion or myotomy alone (*Table 1*). Excision was performed from 1966 until 1977 but after re-examining the historical arguments of fewer complications and a shorter hospital stay after inversion, this method was adopted from 1978. Three patients had different operations: one had a Dohlman's endoscopic diathermy, another a total pharyngolaryngectomy for a carcinoma of the pouch, and the last had pharyngeal reconstruction with a deltopectoral flap for a complete stenosis following an excision elsewhere.

The ages of the 53 patients who underwent surgery ranged from 38 to 92 years with a median of 63 (*Table 1*). There were 37 men and 16 women, a ratio of 2·3 to 1. These figures are comparable with most other personal series[9–12]. Two patients had a carcinoma of the diverticulum, an incidence of 3·7 per cent which is similar to other series[13,14].

The typical symptom pattern of dysphagia, regurgitation and weight loss was found in most patients, with duration of symptoms varying between 6 months and 20 years, with a mean of 40·7 months. Nocturnal coughing was present in nine cases, all of whom had either medium or large diverticula.

The 50 patients in the three main groups described were reviewed. Each patient was asked to attend a follow-up appointment, or to answer a questionnaire (*Figure 1*): 31 answers were received. Of the remaining 19 patients, 10 had died and 9 could not be traced either through their old addresses or through the general practitioner.

Operative technique for inversion

The technique that we have used is the same as the one-stage excision up to the point of completion of mobilization of the sac to its neck, with exposure through a horizontal incision at the level of the cricoid cartilage on the left hand side. At this point a stay suture is inserted inferiorly and superiorly to the neck of the sac which is then inverted from the fundus into the lumen of the oesophagus. Holding it in this position with a pair of non-toothed forceps, the serosa around the neck of the sac is closed in from side to side with a continuous chromic catgut suture. A second layer of interrupted sutures is then inserted to re-inforce the closure.

A cricopharyngeal myotomy is performed in the usual manner,

Table 1 *Clinical data*

	No. of cases	Sex M	Sex F	Age (median)	Symptoms (duration in months)	Hospital stay (median in days)
Excision	21	18	3	63	38	10
Inversion	20	14	6	60	37	7
Myotomy	9	4	5	70	46	5
Total	50	36	14	63	39	8

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BEFORE YOUR OPERATION

1. How many years had you had problems (symptoms) with the pouch ....
2. Did you lose weight YES/NO
   If YES, how much ....
3. Did your meals take longer to eat YES/NO
4. Did your breath smell YES/NO
5. Did you notice a swelling in your neck YES/NO
6. Did you hear any gurgling in your neck YES/NO
7. Did you regurgitate undigested food YES/NO

   If YES was it with SOLIDS
   SEMI-SOLIDS
   FLUIDS
   (Ring correct answer)
8. Did you notice any hoarseness YES/NO
9. Did you have difficulty swallowing YES/NO

   If YES was it with SOLIDS
   SEMI-SOLIDS
   FLUIDS
   (Ring correct answer)
10. Did you splutter, or choke with eating YES/NO
11. Did you wake in the night choking or coughing YES/NO
12. Did you have any other symptoms YES/NO

    If YES please state their nature in the space below.
13. When was the diagnosis first discovered (year) ....
14. Where was the diagnosis first discovered (Hospital) ....
15. Was the diagnosis made by a barium X-ray YES/NO

    If NO how was it made ....
16. When was your operation..... month..... year
17. Did you have any complications whilst in hospital YES/NO

    If YES do you recall their nature and if so state below
18. How long were you in hospital .... days
19. Have you had any problems (symptoms) since your operation YES/NO

    If YES could you refer back to questions 2–12 and put down here those numbers that you have had with any additional information you think helpful.
20. Have you had further treatment or operation YES/NO

    If YES could you state what it was and where it occurred and by whom/when

Figure 1 *The questionnaire sent to the patients included in the study*

Table 2 *Complications and deaths*

	Excision (21 patients)	Inversion (20 patients)	Myotomy (9 patients)
Wound infection	2	2	0
Chest infection	2	2	0
Fistula	4	1	0
Vocal cord palsy	1	1	0
Death	2	0	0
Totals	11 (52%)	6 (30%)	0

haemostasis achieved and the wound closed in two layers with continuous chromic catgut and interrupted Prolene (Ethicon Ltd, UK), with a separate suction drain.

The nasogastric tube, inserted during preliminary oesophagoscopy, is left *in situ* until the following morning and is then removed provided that the patient experiences no difficulty with swallowing. We have operated on sacs of all sizes by this technique, without experiencing any difficulties in patient recovery.

Results

The patients in the study were assessed as separate groups and as a whole. The age, sex, duration of symptoms before treatment, and length of hospital stay are shown in *Table 1*. The operative and postoperative complications are shown in *Table 2*. The patients undergoing excision and cricopharyngeal myotomy experienced the most complications, in particular serious complications such as fistula, as well as the highest mortality, whereas those having inversion and myotomy had fewer complications and no mortality, and those having myotomy alone no complications or mortality.

Table 3 *Symptoms of recurrence*

	No.	%
Excision	6/19	31·6
Inversion	2/20	10
Myotomy	1/9	11
Total	9/48	18·8

Table 3 shows the recurrence of symptoms and diverticula in the three groups. Again the highest recurrence rate was found in the excision and myotomy group, with six patients having symptoms, one of whom had a radiologically confirmed recurrence. Of the nine patients who had symptomatic recurrence, two patients, both in the excision group, were 'high risk' patients having undergone previous excision elsewhere.

There was a median follow-up period of 6 years for all methods, but on separate analysis it was 11 years (range 4–19 years) for excision, 3 years (range 2–8 years) for inversion, and 2 years (range 1–6 years) for myotomy alone.

One major factor in this population of patients was the second referral rate, nine of the patients having been sent from other hospitals after unsuccessful surgery. Three of these patients were in the inversion group and six in the excision group; however, this did not significantly alter the complication rate which was 31·7 per cent for the 41 patients seen primarily in the unit, and 33 per cent for the 9 patients from elsewhere. The whole group of 50 patients had a complication rate of 34 per cent. The mortality rate was 4 per cent for the whole group, though both deaths were in the excision group, the first a 73-year-old man who died of pneumonia 10 days postoperatively, and the second a 71-year-old man who died of a myocardial infarction at home 4 weeks after surgery. There was one case of a carcinoma *in situ* arising in a diverticulum.

The complications from both excision and inversion tended to present at a greater age than the median age of each group, at 64 years old and 63·5 years old respectively.

Most significant was the median hospital stay for each group, which was 5 days for myotomy alone, 7 days for inversion and myotomy, and 10 days for excision and myotomy.

Discussion

In our series the mortality rate was 4 per cent for all 50 patients, and in other reports ranges from 0·45 to 8·3 per cent[15–19], though frequently death results from cardiac or pulmonary complications rather than directly from the diverticula complications. The morbidity for our patients was 52 per cent for excision, and 30 per cent for inversion with an overall figure of 34 per cent. The range in other reports is from 6·2 to 53 per cent[15,18–23]. The wide range is in part due to whether all possible complications are listed, and standardization of reporting would facilitate better evaluation of different techniques. One of the main contra-indications is in the elderly and unfit, where previously the Dohlman's technique has been favoured due to the alleged brevity and safety of the procedure[24,25]. However it has many drawbacks, not least of which is that although each procedure is brief most patients require two or more operations before adequate relief of symptoms is achieved[13,23,26]. Furthermore, there is a risk of mediastinitis[27], and of missing a carcinoma by not removing the predisposing factors to carcinomatous change[11,13,26,28]. This present philosophy is maintained by recent papers which compare one-stage excision with Dohlman's procedure[29,30].

The complications of excision include infection, fistula, and mediastinitis, all of which are far less likely to result from an operation that does not breach the mucosa. In this manner inversion has a distinct advantage over either one-stage excision or endoscopic division of the septum. The only apparent disadvantage is the temporary symptom of a lump in the throat that some patients experience, but this usually settles by the third or fourth day postoperatively. The patients can safely be allowed to drink on the first postoperative day, and even to eat, and can go home within 48 h.

Recurrence following surgery varies between 3 and 23 per cent[10,15,16,19,22] but this generally refers to symptomatic recurrence. Gullane *et al.*[10] reported a 55 per cent recurrence rate from radiographic assessment, though only a 28·6 per cent on subjective symptoms. Bertelsen and Aasted[9] reported a 2 per cent symptomatic recurrence rate in their series but suggested that a 10–12 per cent radiological recurrence rate might be present. Gammelgaard[31] found 14 out of 20 patients had radiological recurrences at up to 8 years following diverticulectomy without myotomy.

In our series, nine patients had undergone previous surgery and required re-exploration, but although mobilization of the diverticulum is technically more demanding it did not lead to a higher complication rate in this sub-group, possibly because of increased awareness of the risks.

The figures for recurrence of symptoms and definitive diverticulum are comparable to other series as a whole (*Table 3*), but are lower for those patients who underwent inversion (10 per cent) rather than excision (31·6 per cent). However, one point that requires stressing is the need for careful inspection by oesophagoscopy in patients having inversion to exclude a carcinoma, as the diverticulum is not being removed although it does atrophy. There are few series that describe the use of inversion though Escher[32], in his series of 40 inversions, had one death from heart failure and one fistula. More recently Freeland and Bates[33] treated nine patients by inversion of the sac with no recorded complications postoperatively, a hospital stay of only 4 days against 16 for excision, and a shorter operation time.

In conclusion we feel that the operation of inversion of a diverticulum is safer, results in a shorter hospitalization, may be used on any size of sac and is the best surgical alternative in the management of posterior pharyngeal pulsion diverticula.

References

1. Ludlow A. A case of obstructed deglutition, from a preternatural dilatation of, and bag formed in the pharynx. *Medical Observations and Enquiries* 1769; **3**: 85–101.
2. Wheeler WI. Pharyngocoele and dilation of pharynx, with existing diverticulum at lower portion of pharynx lying posterior to the oesophagus, cured by pharyngotomy, being the first case of the kind recorded. *Dublin J Med Sci* 1886; **82**: 349–56.
3. Stetten D. The radical extirpation of pharyngo-oesophageal pressure diverticula. *Ann Surg* 1910; **51**: 300–19.
4. Girard C. Du traitement des diverticules de l'oesophage. *Cong Franc de Chir* 1896; **10**: 392–407.
5. Halstead AE. Diverticula of the oesophagus. *Ann Surg* 1904; **39**: 171–93.
6. Bevan AD. Pulsion diverticulum of the oesophagus—cure by the Sippy-Bevan operation. *Surg Clin N Amer* 1917; **1**: 449–57.
7. Goldman EE. Die zweizerfge operation von Pulsiondivertikeln der Speiserohre. *Bertr Klin Chir* 1909; **61**: 741–9.
8. Lahey FH. Esophageal diverticula. *Surg Gynecol Obstet* 1954; **98**: 1–28.
9. Bertelsen S, Aasted A. Results of operative treatment of hypopharyngeal diverticulum. *Thorax* 1976; **31**: 544–7.
10. Gullane PJ, Willet JM, Heeneman H, Greenway RE, Ruby RRF. Zenker's diverticulum. *J Otolaryngol* 1983; **12**: 53–7.
11. Juby HB. The treatment of pharyngeal pouch. *J Laryngol Otol* 1978; **92**: 1101–15.
12. Shallow TA, Clerf LH. One stage pharyngeal diverticulectomy. *Surg Gynecol Obstet* 1948; **86**: 317–22.
13. Dohlman G, Mattson O. The endoscopic operation for hypopharyngeal diverticula. *Arch Otolaryngol* 1960; **71**: 744–52.
14. Lindskog GE, Stern H. Diverticulum of the oesophagus. *Yale J Biol Med* 1954; **26**: 285–94.
15. Barichello AW, Nanson EM. Pharyngeal diverticulum. *Canad J Surg* 1970; **13**: 5–8.
16. Boyd DP, Adams HD. Esophageal diverticulum. *New Engl J Med* 1961; **264**: 641–5.
17. Holinger PH, Schild JA. The Zenker's (hypopharyngeal) diverticulum. *Ann Otol Rhinol Laryngol* 1969; **78**: 679–88.
18. Mortensen JD, Clagett OT, Schmidt HW, Gray HK. One stage esophageal diverticulectomy. *J Thorac Cardiovasc Surg* 1955; **30**: 316–22.
19. Payne WS, Clagett OT. Pharyngeal and esophageal diverticula. *Curr Probl Surg* (*Chicago*) 1965; (April) 1–31.
20. Butcher PB, Larrabee WP. Surgical treatment of hypopharyngeal (Zenker's) diverticulum. *Arch Otolaryngol* 1979; **105**: 254–7.
21. Eastridge CE. Pharyngo-esophageal diverticulum. *South Med J* 1972; **65**: 745–8.
22. Finney GG, Gaertner RA. Surgical treatment of pharyngo-esophageal diverticula. *South Med J* 1964; **57**: 375–8.
23. Todd GB. The treatment of pharyngeal pouch. *J Laryngol Otol* 1974; **83**: 307–15.
24. Dohlman G. Endoscopic operations for hypopharyngeal diverticula. *Proc 4th Internat Cong Otolaryngol* (*London*) 1949; **2**: 715–17.
25. Van Overbeek JJM. Endoscopic treatment of the hypopharyngeal diverticulum. *Laryngoscope* 1982; **92**: 88–91.
26. Mackay IS. The treatment of pharyngeal pouch. *J Laryngol Otol* 1976; **90**: 183–90.
27. Hansen JB, Gundtoft JP, Sorensen HR. Pharyngo-esophageal diverticula. *Scand J Thorac Cardiovasc Surg* 1973; **7**: 81–9.
28. Turner MJ. Carcinoma as a complication of pharyngeal pouch. *Br J Radiol* 1963; **36**: 206–10.
29. Trible WM. The surgical treatment of Zenker's diverticulum: endoscopic vs external operation. *South Med J* 1975; **68**: 1260–2.
30. Welch AR, Stafford F. Comparison of endoscopic diathermy and resection in the surgical treatment of pharyngeal diverticula. *J Laryngol Otol* 1985; **99**: 179–82.
31. Gammelgaard A, Esophageal diverticula. *Acta Chir Scand* 1955; **109**: 181–3.
32. Escher F. Zur therapie des Zenkershen Divertikels. *Schweiz Med Wschr* 1984; **114**: 1428–33.
33. Freeland AP, Bates GJ. The surgical treatment of a pharyngeal pouch: inversion or excision. *Ann R Coll Surg Eng* 1987; **69**: 57–8.

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Hazards of thrombolytic therapy in deep vein thrombosis

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From 1965 to 1985, 64 deep vein thrombosis (DVT) patients were treated with streptokinase (SK). In 26 cases 'high-dose SK' (IV 100 000 units/h for 4 days) was used and in 38 patients a 'low-dose SK' regime (IV 250 000 units every 12 h for 4 days) was employed. The clinical signs of DVT subsided in 78 per cent of treated patients within 30 days of completing SK treatment. A repeat phlebography was performed immediately after SK therapy in 29 patients (45 per cent) and a total recanalization or partial thrombolysis was achieved in 80 per cent of the studied cases. In 15 patients minor and major haemorrhagic complications occurred. There were five fatalities, all in the high-dose SK group (three intracranial haemorrhages and two major bleeds). Three patients developed pulmonary embolism and none of them died. The post-treatment clinical and phlebographic evaluation did not reveal any significant difference between the two methods of SK administration, but more haemorrhagic complications ($P<0{\cdot}02$, $\chi = 5{\cdot}50825$) *occurred in the high-dose SK patients. This report emphasizes the risk of bleeding complications during thrombolytic therapy. If SK is to be used, therefore, careful selection of patients and meticulous monitoring are mandatory.*

Keywords: Streptokinase treatment, thrombolysis, deep vein thrombosis

The main therapeutic objectives of fibrinolytic therapy in deep vein thrombosis (DVT) are prevention of pulmonary embolization, thrombus propagation and postphlebitic syndrome, as well as the promotion of thrombus resolution and restoration of normal venous circulation in the affected veins. The comparative studies show that lysis of deep vein thrombus is achieved in 61 per cent of patients after streptokinase (SK) treatment but in only 18 per cent after heparin therapy[1–3]. Several multi-institutional and individual randomized studies on the effectiveness of conventional SK therapy in DVT have been performed and the clinical results were shown to be excellent in 42–82 per cent and radiological improvement at follow-up periods ranging from 1 to 82 months was noted in 42–86 per cent[4–8]. The incidence of chronic venous insufficiency was found to be much lower among DVT patients in whom a complete lysis of thrombi was achieved following SK therapy[9,10]. Currently there is no substantial evidence that standard phlebography and routine clinical examination are the only reliable means of assessment of the valvular function restoration in patients with a post-thrombotic leg. There is evidence in the literature that phlebographic resolution of the proximal thrombi and absence of the leg ulcer or severe post-thrombotic syndrome does not necessarily mean that sufficient valvular function has been restored after conventional SK therapy. Furthermore, functional studies on the post-thrombotic leg have revealed that only 6 per cent of DVT patients treated with SK were free from symptoms and signs of valvular insufficiency[11,12].

Bleeding is the major complication of SK administration as both pathological thrombi and physiologically formed clots are equally affected by the lytic process. The risk factors for haemorrhage in patients receiving fibrinolytic agents are well known. Nevertheless, even reliable laboratory tests of the clotting mechanism and careful patient selection and management do not eliminate the hazards of unexpected and severe complications during and after SK treatment[2,3,13–16].

The aim of this study was to assess the clinical effectiveness of fibrinolytic therapy and to analyse the complications of thrombolytic therapy in DVT patients treated in the Department of Surgery of the Institute of Haematology in Warsaw from 1965 to 1985.

Patients and methods

The study included 64 patients (mean age 48·4 years, range 18–79 years) with clinical evidence of DVT of the lower or upper limbs. The mean duration of the signs of DVT was 8·4 days (range 2–21 days). Clinical signs of DVT were evaluated daily during the SK treatment and then once weekly after thrombolytic therapy was completed. Ascending phlebography was performed by the method of Rabinov and Paulin[17], modified with a tourniquet around the ankle, before treatment and between days 3 and 24 after termination of SK administration. The radiological findings obtained from control phlebograms were classified as total recanalization, partial thrombolysis or lack of thrombolysis. Anatomical distribution of thrombi as determined by phlebographic studies is presented in *Table 1*.

Heparin (Polfa, PL) 5000 units IV was initially given to all patients and repeated in doses sufficient to increase the activated partial thromboplastin time (APTT) from 1·5 to 2·5 times until the clinical diagnosis of DVT had been confirmed by phlebographic studies. Hydrocortisone 100 mg IV was given before the first loading dosage of streptokinase (Streptokinaza Biomed PL, Kabikinase Kabi D, Streptase Behringwerke D).

In the period from 1965 to 1975 all DVT patients admitted to the surgical ward were given conventional high-dose SK therapy and from 1975 they were allocated to either high-dose or low-dose SK treatment.

The high-dose SK treatment was instituted in 26 patients (group A). The initial loading dose of 500 000 units in 100 ml of 5 per cent dextrose

Table 1 *Anatomical distribution of thrombi as determined by phlebography*

	Method of SK administration	
Veins	High dose	Low dose
Iliac + femoral	2	2
Iliac + femoral + popliteal + tibial	3	—
Femoral	2	4
Femoral + popliteal + tibial	10	10
Popliteal + tibial	1	4
Tibial	5	9
Phlegmasia cerulea dolens	2	—
Subclavian + axillary + brachial	1	9
Total number of patients	26	38

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Table 2 *Complications observed among 64 DVT patients treated with streptokinase and heparin*

Complication	SK administration (dosage) High	SK administration (dosage) Low	Heparin (post-SK course)
Intracranial haemorrhage and haematoma of the thigh	1		
Intracranial haemorrhage	1		1
GI bleeding	1		
Intramuscular haematoma	1	2	1
Wound haematoma	1		
Retroperitoneal haematoma	1		
Haematuria		1	1
Iliac region haematoma	1		
Epistaxis		1	
Pulmonary embolism	2		1
Pulmonary embolism and epistaxis		1	
Number of complications	9	5	4

was given intravenously over 30 min. Continuous IV SK administration was then maintained at a dose of 100 000 units/h for 4 days.

The low-dose SK treatment was instituted in 38 patients (group B). The initial loading dose of 500 000 units in 100 ml of 5 per cent dextrose was given intravenously over 30 min. The subsequent maintenance doses of 250 000 units in 100 ml of 5 per cent dextrose were given intravenously over 15 minutes every 12 h for 4 days.

In all patients heparin was given by continuous IV administration after SK therapy and was maintained for 5 days. The dosage of heparin was altered in order to increase the APTT from 1·5 to 2·5 times. Treatment with oral anticoagulants (Sintrom Geigy CH, Syncumar Alkaloida H) was started 3 days after the initiation of heparin therapy and was maintained for 3–6 months.

The course of SK, heparin and oral anticoagulant therapy was monitored by coagulation laboratory with thrombin, prothrombin, activated partial thromboplastin times, fibrinogen plasma level, haematocrit and platelet count.

During the first 10 days of treatment the patients were immobilized in bed with the affected limb raised.

Results

Out of 64 patients, 7 were excluded from the clinical follow-up studies (5 fatal cases and in 2 early discontinuation of SK administration). The presence on average of four clinical signs—local tenderness, increased tissue turgor, swelling and Homan's sign—was noted in 57 patients before the SK treatment. On the third day of SK administration a mean of only two signs (swelling and increased tissue turgor) were observed in 50 per cent of treated patients. Thirty days after termination of SK therapy 78 per cent of patients were free from DVT signs. The rate of subsidence of the clinical signs of DVT in group A (high-dose SK) and group B (low-dose SK) did not differ during and after administration of SK.

At the end of treatment 29 patients (45 per cent) were examined by phlebography; the remaining were not available: 5 patients died, in 6 the SK treatment was interrupted, in 12 radiographs were missing and in 12 the control phlebography was not done because of technical difficulties. Total recanalization was shown in 10 of the 29 patients studied (1 in group A and 9 in group B) and partial thrombolysis in 13 cases (8 in group A and 5 in group B). No evidence of thrombolytic effect was found in six patients (one in group A and five in group B).

In 17 patients (26·5 per cent) febrile reactions (a mean of 39°C) were associated with SK administration. Twenty-nine patients (45 per cent) suffered from minor bleeding from the venopuncture sites during the course of SK and heparin treatment.

In 15 patients (23·4 per cent), mean age 55 years (range 25–78 years) minor and major haemorrhagic or embolic complications occurred. In three patients more than one complication was observed. The list of complications during SK treatment is presented in *Table 2*. The mean time between initiation of SK administration and clinical manifestation of a complication was 41·5 h (range 12–96h). The results of the tests of haemostasis assessed on the day of complication are listed in *Table 3*.

There were five deaths (7·8 per cent of total number of sixty-four patients), all of which were in group A (high-dose SK administration). In three patients (mean age 55·6 years, range 44–66 years) a cause of death was intracranial haemorrhage, two of which occurred at the twenty-fourth and sixty-fourth hour of the SK treatment and one on the second day of the post-SK heparin course. The past history and clinical examination prior to SK therapy did not reveal cerebrovascular disease and CNS abnormalities. Medical treatment was unsuccessful and the patients died on the third day (pulmonary oedema, respiratory insufficiency), on the nineteenth day (respiratory insufficiency) and on the sixtieth day (bilateral pneumonia and acute cardiac failure), respectively. In the fourth case a massive retroperitoneal haematoma developed on the third day of SK administration; thrombolytic treatment was immediately discontinued. The patient did not improve after restoration of blood volume with packed RBC and frozen plasma transfusions. The clinical course was complicated by acute liver failure which led to encephalopathy and he died on the twenty-first day after haemorrhage occurred. Carcinoma of the pancreas was found on autopsy with massive haematoma in the left retroperitoneal space. The fifth fatal case was a 60-year-old woman who developed a massive haematoma in the postoperative wound after embolectomy of the right iliac artery. DVT of the left calf veins and popliteal vein was diagnosed on the fourth postoperative day and the SK treatment was initiated. The signs of the wound haematoma occurred 12 h later; the patient became hypotensive, and in spite of massive blood transfusions she died 6 h later. A post-mortem examination revealed a large haematoma in the right iliac fossa and thrombi in the left atrium. In the remaining ten patients we observed twelve complications—nine haemorrhagic and three embolic. In three cases (massive haematuria, GI bleeding and a large haematoma in the gluteal region) SK administration was discontinued and all patients required blood transfusions (mean 5 units of blood per patient). In three patients SK therapy was discontinued, no blood was given and in the remaining three cases (small subcutaneous haematoma of the arm, epistaxis and haematoma of the abdominal wall) SK therapy was continued as planned. In five out of six patients in whom the SK treatment was discontinued, administration of oral anticoagulants was initiated 96 h after the onset of the bleeding episodes without further complications.

Three patients developed symptoms and signs of pulmonary embolism while on the SK and heparin treatment: none of them died. One patient required respiratory support for 18 h as he developed recurrent embolism while on heparin. The SK therapy was completed as planned in all cases. The diagnosis of pulmonary embolism was confirmed by clinical, laboratory and radiological studies.

Table 3 *The mean values of coagulation tests performed on the day of complication in 15 patients. Numbers in parentheses indicate normal laboratory values*

Test	Patients Non-fatal group	Patients Fatal group
Platelet count ($\times 10^9$/l) (150–350 $\times 10^9$/l)	124·6	93·6
Fibrinogen level (μmol/l) (4·0–8·0 μmol/l)	1·0	0·7
Thrombin time (s) (15–17 s)	40·0	65·0
APTT (s) (35–46 s)	63·5	74·0

Discussion

In 64 patients the diagnosis of DVT was established on clinical and radiological findings. Two regimens of thrombolytic therapy were instituted with 'high dose' and 'low dose' streptokinase. The clinical signs of DVT subsided in 78 per cent of treated patients within the 30-day period after the full course of thrombolytic therapy was completed. Total recanalization or partial thrombolysis was documented by phlebography in 23 patients (80 per cent of cases studied). Corresponding observations were reported by Elliot[9], Arnesen[1], Kakkar[18] and Ott[3]. Although the follow-up of these patients has shown the beneficial clinical effect of thrombolytic therapy the non-randomized and retrospective character of this study does not allow us to determine which of the two methods of SK administration was more successful.

The most common complication of SK therapy in this series was an unpredictable haemorrhage which was independent of fibrinogen level and thrombin time, with values kept within therapeutic ranges. The frequency of the reports of bleeding complications in patients undergoing thrombolytic therapy is increasing as this method of DVT treatment has been more widely used[3,9,19,20].

Fatal intracranial haemorrhage was observed in three of sixty-four treated patients (4·7 per cent). A similar frequency of intracranial bleeding was reported by Amery[19], Conard[13] and Hess[21]. The pretreatment detection of unsuspected organic or vascular cerebral lesions still remains very difficult. The introduction of computerized tomography into routine clinical practice may reduce the frequency of undiagnosed brain diseases and thus decrease the number of DVT patients accepted for thrombolytic therapy.

Pulmonary embolism was observed in three out of sixty-four treated patients (4·7 per cent). All affected persons survived and the follow-up studies did not reveal symptoms or signs of pulmonary hypertension. Schulman[10] reported one fatal pulmonary embolism in a series of eighty DVT patients undergoing SK therapy. Robertson[22] reported four non-fatal cases of pulmonary embolism out of thirty-one SK-treated patients. Hess[21] observed 1·1 per cent of fatal and 2·9 per cent non-fatal pulmonary embolism cases during SK therapy. Elliot[9] reported one asymptomatic pulmonary embolism during SK treatment out of twenty-six patients. Ott[3] observed nine out of one hundred and eight DVT patients, and three of them (2·8 per cent) died. These data indicate that unpredictable pulmonary embolism occurs during thrombolytic therapy. We therefore recommend institution of SK treatment in the intensive care unit and are of the opinion that pulmonary embolism does not constitute an indication for discontinuation of thrombolytic therapy.

Our experience based on analysis of the results of the treatment of DVT bearing in mind the clinical and phlebographic studies did not reveal any significant difference between the two methods of SK administration; however, more haemorrhagic complications ($P<0{\cdot}02$, $\chi^2=5{\cdot}50825$) and all fatal cases occurred in 'high-dose SK'-treated patients. Moreover, as high-dose SK treatment has not achieved general acceptance and the reported results are still conflicting, the need to determine optimal therapy of DVT is still necessary. Second-generation thrombolytic agents such as tissue-type plasminogen activator, acylated streptokinase–plasminogen complex and single-chain urokinase-type plasminogen activator (pro-urokinase) await full scientific assessment and the precise role of these agents in DVT therapy is yet to be defined.

References

1. Arnesen H, Heilo A, Jakobsen E, Ly B, Skaga E. A prospective study of streptokinase and heparin in the treatment of deep vein thrombosis. *Acta Med Scand* 1978; **203**: 57–63.
2. Goldhaber SZ, Buring JE, Lipnick RJ, Hennekens CH. Pooled analysis of randomized trials of streptokinase and heparin in phlebographically documented acute deep venous thrombosis. *Am J Med* 1984; **76**: 393–7.
3. Ott P, Eldrup E, Oxholm P, Vestergard A, Knudsen JB. Streptokinase therapy in the routine management of deep venous thrombosis in the lower extremities. *Acta Med Scand* 1986; **219**: 295–300.
4. Common HH, Seaman AJ, Rösch J *et al.* Deep vein thrombosis treated with streptokinase or heparin. *Angiology* 1976; **27**: 645–54.
5. Johansson E, Eicson K, Zetterquist S. Streptokinase treatment of deep venous thrombosis of the lower extremity: clinical, phlebographic and plethysmographic evaluation of early and late results. *Acta Med Scand* 1976; **199**: 89–94.
6. Kakkar VV, Howe CT, Laws JW *et al.* Late results of treatment of deep vein thrombosis. *Br Med J* 1969; **1**: 810–11.
7. Mavor GE, Dhall DP, Dawson AA *et al.* Streptokinase therapy in deep vein thrombosis. *Br J Surg* 1973; **60**: 468–74.
8. Widmer LK, Mader G, Schmitt HE *et al.* Heparin oder thrombolyse in der Behandlung der tiefen Beinvenen Thrombose. *Vasa* 1974; 3: 422–32.
9. Elliot MS, Immelman EJ, Jeffery P *et al.* A comparative randomized trial of heparin versus streptokinase in the treatment of acute proximal venous thrombosis: an interim report of a prospective trial. *Br J Surg* 1979; **66**: 838–43.
10. Schulman S, Lockner D, Granquist S, Bratt G, Paul Ch, Nyman D. A comparative randomized trial of low-dose versus high-dose streptokinase in deep vein thrombosis of the thigh. *Thromb Haemostas* 1984; **51**: 261–5.
11. Albrechtsson U, Anderson J, Einarsson E, Eklöf B, Norgren L. Streptokinase treatment of deep venous thrombosis and the postthrombotic syndrome. *Arch Surg* 1981; **116**: 33–7.
12. Norgren L, Widmer LK. Venous function evaluated by foot volumetry in patients with a previous deep venous thrombosis treated with streptokinase. *Vasa* 1978; **7**: 412–14.
13. Conard J, Samama M *et al.* Complications hemorrhagiques au cours de 98 traitments par la streptokinase. *Nouv Presse Med* 1979; **16**: 1319–25.
14. Marder VJ. The use of thrombolytic agents: choice of patient, drug administration, laboratory monitoring. *Ann Intern Med* 1979; **90**: 802–8.
15. Persson AV, Robichaux WT, Jaxheimer EC, DiPronio EM. Burst therapy: a method of administering fibrinolytic agents. *Am J Surg* 1984; **147**: 531–6.
16. Urokinase–Streptokinase Pulmonary Embolism Trial Study Group: The urokinase–streptokinase pulmonary embolism trial: phase II results. *J Am Med Ass* 1974; **229**: 1606–13.
17. Rabinov K, Paulin S. Roentgen diagnosis of venous thrombosis in the leg. *Arch Surg* 1972; **104**: 134–44.
18. Kakkar VV, Flanc C, Howe CT *et al.* Treatment of deep vein thrombosis. A trial of heparin, streptokinase and arvin. *Br Med J* 1969; **1**: 806–10.
19. Amery A, Deloof W, Vermylen J, Verstraete M. Outcome of recent thrombolytic occlusion of the limb arteries treated with SK. *Br Med J* 1970; 4: 639–44.
20. Stolberg L, Fix K. Blood loss after thrombolytic therapy. *West J Med* 1985; **142**: 698.
21. Hess H, Ingrish H, Mietaschk A, Rath H. Local low-dose thrombolytic therapy of peripheral occlusion. *N Engl J Med* 1982; **307**: 1627–30.
22. Robertson BR, Nilsson IM, Nylander G. Thrombolytic effect of streptokinase as evaluated by phlebography of deep venous thrombi of the leg. *Acta Chir Scand* 1970; **136**: 173–80.

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Effect of carotid endarterectomy on cerebral blood flow and its response to hypercapnia

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Cerebral blood flow (CBF) was measured in 14 patients before carotid endarterectomy, 3 h after surgery and 2 days postoperatively using the intravenous xenon-133 technique. In 11 of the patients CBF was remeasured at 6 months and in 8 patients CBF and the response to hypercapnia (5 per cent CO_2 in air) was measured pre-operatively and 6 months following surgery. All operations were performed using an intraluminal Javid shunt and internal carotid artery (ICA) 'stump' pressure was recorded. CBF measured at 3 h after endarterectomy revealed a postoperative cerebral hyperperfusion with significantly increased flows in both hemispheres. There was a significant correlation between carotid cross clamping time and ipsilateral hemispheric CBF increase which implied an ischaemic aetiology for the hyperperfusion and supported the routine use of an intraluminal shunt in carotid endarterectomy. Six months after surgery, CBF had returned to its pre-operative value but reactivity to CO_2 was significantly improved, which suggested that the operation had increased cerebral reserve.

Keywords: Carotid endarterectomy, cerebral blood flow, hypercapnia

Since the first carotid endarterectomy was reported[1], the procedure has been widely performed. It is estimated that 100 000 such operations are performed annually in the USA making it the most common peripheral vascular operation. Despite these large numbers of operations the effects of carotid endarterectomy on the cerebral circulation remain obscure. Cerebral blood flow (CBF) has been measured before and after carotid endarterectomy during the operation by intracarotid injection of xenon-133[2,3] and found to increase after the removal of a tight stenosis.

Sundt and his colleagues[4] believe that an excessive postoperative cerebral hyperperfusion can cause a form of unilateral encephalopathy with intracerebral haemorrhages (especially if the patient is anticoagulated), fits and migraine attacks, preceded by unilateral headaches. The mechanism of such symptoms is uncertain. Three patients who had convulsions following carotid endarterectomy have been reported[5] but these symptoms were ascribed to embolism rather than hyperaemia. Bernstein and Fleming found similar changes to those seen in hypertensive encephalopathy at autopsy in a patient who had seizures and a fatal intracerebral haemorrhage 6 days after carotid endarterectomy[6]. Sundt has suggested that the hyperaemia is secondary to a loss of cerebral autoregulation[4].

The available data on CBF after carotid endarterectomy are conflicting. Five studies report the long-term effect of carotid endarterectomy on CBF, three of which do not state the interval between the operation and the second measurement. Two studies reported no change in CBF; one using the Kety–Schmidt nitrous oxide method[7] and the other employing the xenon inhalation method[8]. The third study recorded an increase in CBF following carotid endarterectomy[9]. Another study, using the nitrous oxide method, showed an increased CBF 1 month after operation, in patients who had improved clinically and a decrease in patients who had not improved[10]. Herrschaft *et al.*, using the intracarotid xenon method, studied 49 patients 4–6 weeks after endarterectomy[11] and found an increase in CBF.

Using a mobile unit (Novo Cerebrograph) to make frequent sequential studies, Schroeder *et al.* reported the CBF changes of a single patient following carotid endarterectomy[12]. They noted a marked bilateral increase in hemispheric CBF which was maximal 3–4 h after surgery and this then returned to normal in 1 week. We have used a Novo Cerebrograph to record CBF changes after carotid endarterectomy, both in the short-term (3 h and 2 days) and in the long-term (6 months) with the aim of clarifying the postoperative changes in CBF and elucidating the cause of the previously reported short-term cerebral hyperperfusion. Hypercapnia has been used in this study to investigate the effect of the operation on cerebral autoregulation.

Patients and methods

Patients

Fourteen patients (twelve men, two women) undergoing unilateral carotid endarterectomy were studied. Their mean age was 60 ± 5 years (range 46–68). The indication for surgery was amaurosis fugax in nine patients and arm or leg transient ischaemic attacks in five patients. On the basis of pre-operative angiography (IV DSA) and Duplex ultrasound scanning (Philips SDD 500 continuous wave Doppler Scanner with a 5 MHz probe), the operated internal carotid artery (ICA) was tightly stenosed (peak frequency of stenosis > 10 kHz on Doppler scanning) in ten patients and moderately stenosed in four patients (peak frequency of stenosis > 4 kHz but < 10 kHz). The opposite (unoperated) ICA was occluded in two patients, tightly stenosed in two patients, moderately stenosed in five patients and normal (peak frequency of stenosis < 4 kHz) in five patients.

Methods

CBF (ml 100 g^{-1} min^{-1}) was measured by the intravenous injection of approximately 10 mCi of xenon-133 and extracranial recording of isotope clearance by five scintillation detectors positioned over each hemisphere (Novo Cerebrograph 10a Novo Diagnostic Systems, Vertec Scientific, Slough, Berkshire, UK). Hemispheric CBF was calculated from the means of a 1 min initial slope analysis of the five clearance curves. End expiratory xenon concentration was continuously monitored to allow for the effect of arterial circulation. CBF was measured in all 14 patients before carotid endarterectomy, 3 h following surgery and 2 days postoperatively. In 11 patients CBF was also measured 6 months after operation.

The response of CBF to hypercapnia (5 per cent CO_2 in air) was measured pre-operatively and 6 months after surgery in eight patients. End expiratory P_{CO_2} was continuously monitored using a PK Morgan (Gillingham, Kent, UK) 901-2 infrared CO_2 analyser and plotted by a

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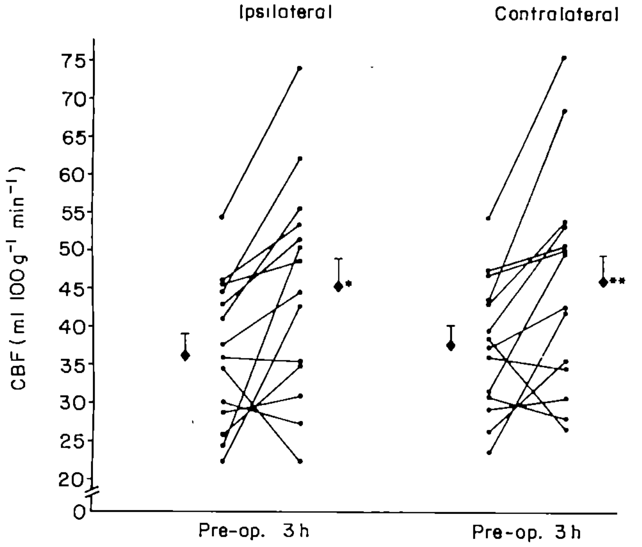

Figure 1 *Change in CBF (ml 100 g^{-1} min^{-1}) 3 h after carotid endarterectomy in the ipsilateral and contralateral hemisphere. Diamonds refer to means ± s.e.m.* *$P<0·01$, **$P<0·05$ *(paired* t *test)*

pen recorder. The response of CBF to hypercapnia was expressed as a reactivity index: percentage increase in hemispheric CBF (ml 100 g^{-1} min^{-1}) per mmHg change in end expiratory P_{CO_2}.

Blood pressure was recorded automatically during both the normocapnic and hypercapnic CBF studies using a Critikon Dinamap sphygmomanometer (Critikon Ltd, Sunningdale, Berkshire, UK).

During the endarterectomy the cerebral circulation was maintained with an indwelling shunt (Javid) in all cases. Internal carotid artery occlusion and shunting times were recorded. The nerve to the carotid sinus was blocked with 5–10 ml of 1 per cent plain lignocaine. Five thousand units of heparin was given intravenously before carotid occlusion and reversed with 50 or 25 mg protamine sulphate at the end of the operation. The arteriotomy in the common carotid artery was closed with 5/0 Prolene (Ethicon Ltd, UK) sutures, the internal carotid arteriotomy was closed with 6/0 Prolene. Vein or Dacron® (C. R. Bard Inc., Massachusetts, USA) patches were not used.

The ICA 'stump' pressure was measured in all patients before the placement of the Javid shunt.

The patients were not premedicated before surgery. General anaesthesia was induced with thiopentone 4 mg kg^{-1}, fentanyl 2 mg kg^{-1} and suxamethonium 100 mg to facilitate intubation. Following pancuronium 0·1 mg kg^{-1}, IPPV was instituted with nitrous oxide, oxygen and Ethrane (Abbott Laboratories Ltd, UK), using a Manley ventilator set at a minute volume of 100–120 ml kg^{-1}. All patients received dexamethasone 40 mg intravenously and one received hydralazine 10 mg to control blood pressure. Intra-operative monitoring consisted of continuous ECG and automated blood pressure recordings. The end tidal carbon dioxide concentration was not measured. Reversal was with neostigmine 5·0 mg and atropine 2·0 mg and the patients woken as quickly as possible for neurological assessment. Postoperative analgesia was achieved with codeine phosphate 30–60 mg IM.

Statistical analysis was performed by linear regression analysis and Student's *t* test using a Litton Monroe 1930 calculator. *P* values derived from regression coefficients were obtained from tables in Documenta Geigy[13].

Results

Pre-operatively the mean CBF in the hemisphere on the side of the carotid endarterectomy was 36·2 ml 100 g^{-1} min^{-1} (s.d. 9·8) and in the opposite hemisphere was 37·3 ml 100 g^{-1} min^{-1} (s.d. 8·8). Three hours after the operation (*Figure 1*), the mean CBF had increased significantly to 45·1 ml 100 g^{-1} min^{-1} (s.d. 14·2) in the ipsilateral hemisphere ($P<0·01$, paired *t* test) and to 45·5 ml 100 g^{-1} min^{-1} (s.d. 14·6) in the contralateral hemisphere ($P<0·05$, paired *t* test). The mean CBF was still raised 2 days after the operation (39·8 ml 100 g^{-1} min^{-1} in the ipsilateral hemisphere and 39·8 ml 100 g^{-1} min^{-1} in the contralateral hemisphere) but this difference was no longer statistically significant from the pre-operative values.

In the 11 patients who had a repeat study 6 months after surgery, the mean hemispheric CBF was not significantly different from the pre-operative value. In the ipsilateral hemisphere, CBF was 36·1 ml 100 g^{-1} min^{-1} pre-operatively and 38·0 ml 100 g^{-1} min^{-1} at 6 months ($P=0·2$) and in the contralateral hemisphere it was 36·4 ml 100 g^{-1} min^{-1} pre-operatively and 38·3 ml 100 g^{-1} min^{-1} at 6 months ($P=0·2$).

The reactivity of the cerebral blood vessels to hypercapnia was significantly greater at 6 months (*Figure 2*). In the ipsilateral hemisphere, the mean reactivity increased from 4·4 to 5·4 ($P=0·03$, paired *t* test) and in the contralateral hemisphere from 4·3 to 5·6 ($P=0·03$, paired *t* test).

When total internal carotid artery occlusion time (the sum of the occlusion time during shunt insertion and the occlusion time needed to remove the shunt and close the arteriotomy) was related to the change in CBF at 3 h (*Figure 3*), there was a significant correlation in the ipsilateral hemisphere ($r=0·5415$, $P<0·05$) but not in the contralateral hemisphere ($r=0·4065$, $P=$ n.s.). The longer the internal carotid artery was occluded the greater was the increase in CBF.

The increase in CBF at 3 h was also compared with the shunting time, the stump pressure, the degree of ipsilateral pre-operative ICA stenosis and the degree of stenosis in the contralateral ICA but no significant correlation was found between any of these measurements.

The mean end expiratory P_{CO_2} was 37·9 mmHg (s.d. 3·0) pre-operatively, 40·5 mmHg (s.d. 2·9) at 3 h, 36·6 mmHg (s.d. 2·6) at 2 days and 38·4 mmHg (s.d. 2·3) at 6 months following carotid endarterectomy.

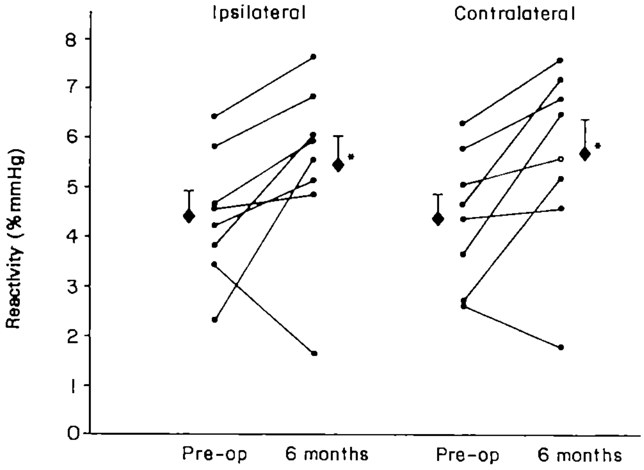

Figure 2 *Change in reactivity (% mmHg) 6 months after carotid endarterectomy in the ipsilateral and contralateral hemisphere. Diamonds refer to means ± s.e.m.* *$P=0·03$ *(paired* t *test)*

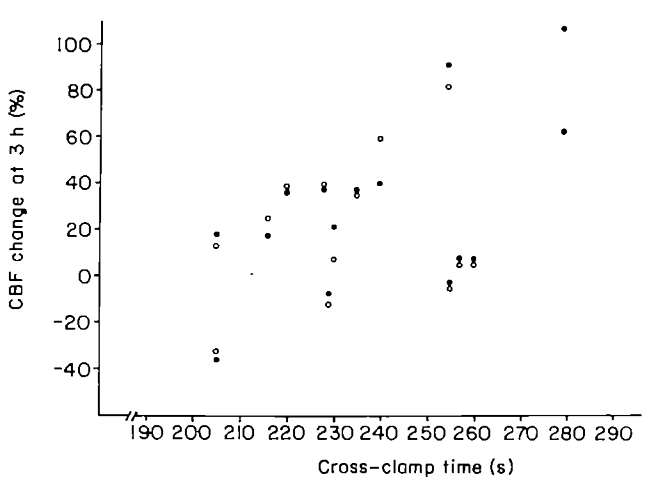

Figure 3 *Percentage change CBF (ml 100 g^{-1} min^{-1}) at 3 h post-carotid endarterectomy compared with carotid cross clamping time (s).* ● *ipsilateral hemisphere* ($r=0·5415$, $P<0·05$), ○ *contralateral hemisphere* ($r=0·4065$, $P=$ *n.s.*)

The mean systolic and diastolic blood pressure was 153/85 peroperatively, 127/72 at 3 h, 140/76 at 2 days and 145/81 at 6 months following carotid endarterectomy.

Discussion

The precise place of carotid endarterectomy in the treatment of carotid atherosclerosis remains controversial[14]. Clinical studies and trials have to be performed on large numbers of patients because the risk of stroke in the population under study is small[15]. This makes it impractical to include CBF measurements in such studies. This paper describes the effect of carotid endarterectomy on CBF in a small group of patients in order to clarify the effect of the operation on the cerebral circulation.

Carotid endarterectomy causes a temporary increase in cerebral blood flow which is similar in both hemispheres (*Figure 1*). This response is probably related to intra-operative ischaemia since we found a significant correlation between total internal carotid artery occlusion time and the increased flow (*Figure 3*). Other factors which might reflect intra-operative ischaemia, such as stump pressure and the state of the contralateral ICA, did not show a significant correlation with the cerebral blood flow increase. The absence of a correlation between the degree of ipsilateral ICA stenosis and CBF suggests that the increased blood flow is not secondary to a long standing reduced cerebral perfusion caused by the stenosis.

The factor mediating the increase in blood flow remains obscure but it could be related to the release of vaso-active substances, such as prostacyclin[16], from the damaged endothelium at the site of the arteriotomy acting on cerebral arterioles which, because of a chronic low perfusion pressure, have lost some of their ability to autoregulate properly.

The increased CBF was not secondary to an increased blood pressure, as the mean blood pressure at 3 h and at 2 days was lower than the pre-operative level. Similarly, the small rise in mean end expiratory P_{CO_2} at 3 h (2·6 mmHg) could not account for the increased CBF measured at that time.

Whether or not this increased blood flow increases the risk of postoperative stroke remains undecided. None of the 14 patients in this study developed headaches or other symptoms of encephalopathy. If, as Sundt *et al.* have suggested[4], postoperative hyperperfusion is detrimental, these studies suggest that a shunt should be used routinely during carotid endarterectomy[17], as this reduces the total carotid cross-clamping time.

The anaesthetic technique used for these operations would be unlikely to be responsible for the increased CBF at 3 h, due to the short half-life of most of the agents used during anaesthesia. Only thiopentone would be present to any large extent 3 h postoperatively and it does not cause cerebral vasodilation. In order to confirm that the anaesthetic technique could not have been responsible for the results, an identical anaesthetic was administered by the same anaesthetist to three patients not having carotid artery cross clamping as part of the operative procedure. In all three there was no change in cerebral blood flow postoperatively.

It is interesting to note that carotid endarterectomy did not increase CBF in the long-term, but the response to hypercapnia significantly increased 6 months after surgery (*Figure 2*). This suggests that these patients were vasodilated in order to compensate for the reduction in perfusion pressure caused by the stenosis, and were therefore unable to respond fully to hypercapnia, pre-operatively. This confirms the view that an ICA stenosis may have a clinically undetected influence on the cerebral circulation, the haemodynamic significance of which may be 'unmasked' by the use of a hypercapnia stress test[18].

These studies have established the existence of a temporary but significant increase of cerebral blood flow after carotid endarterectomy. This is probably secondary to cerebral ischaemia caused by intra-operative clamping of the carotid artery which is necessary to perform the operation. The long-term benefit of the operation in some patients may be related, not to a change in resting blood flow but to an improvement in the cerebrovascular reserve, i.e. the ability to increase CBF in response to hypercapnia and presumably anoxia, in addition to removing the source of cerebral emboli, which are more likely to develop if there is a tight carotid stenosis[19].

Acknowledgements

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References

1. Eastcott HG, Pickering GW, Rob CG. Reconstruction of internal carotid artery in a patient with intermittent attacks of hemiplegia. *Lancet* 1954; **ii**: 994–6.
2. Engell HC, Boysen G, Ladegaard-Pederson HJ, Henriksen H. Cerebral blood flow before and after carotid endarterectomy. *Vasc Surg* 1972; **6**: 14–19.
3. Sundt TM, Sharbrough FW, Anderson RE, Michenfelder JD. Cerebral blood flow measurements and electroencephalograms during carotid endarterectomy. *J Neurosurg* 1974; **41**: 310–20.
4. Sundt TM, Sharbrough FW, Piepgras DG, Kearns TP, Messick JM, O'Fallon WM. Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy. *Mayo Clin Proc* 1981; **56**:9 533–43.
5. Wilkinson JT, Adams HP, Wright CB. Convulsions after carotid endarterectomy. *JAMA* 1980; **244**: 1827–8.
6. Bernstein M, Fleming JFR. Cerebral hyperperfusion after carotid endarterectomy: a cause of cerebral haemorrhage. *Neurosurg* 1984; **15**: 50–6.
7. Adams JE, Smith MC, Wylie EJ. Cerebral blood flow and haemodynamics in extracranial vascular disease: effect of endarterectomy. *Surgery* 1963; **2**: 449–55.
8. O'Brien MD, Veall N, Luck RJ, Irvine WT. Cerebral cortex perfusion rates in extracranial cerebrovascular disease and the effects of operation. *Lancet* 1967; **ii**: 392–5.
9. Obrist WD, Silver D, Wilkinson WE, Harel D, Heyman A, Wang HS. The 133xe inhalation method: assessment of rCBF in carotid endarterectomy. In: Langfitt TW, McHenry LC, Reirich M, Wollman H, eds. *Cerebral Circulation and Metabolism*. New York: Springer Verlag, 1975: 398.
10. Bregentz SE, Haggendal E, Nilsson NJ. Pre and postoperative cerebral blood flow in patients with carotid artery stenosis. In: Brock M, Fieschi C, Ingrav DH, Lassen NA, Schurmann K, eds. *Cerebral Blood Flow*. Berlin: Springer Verlag, 1969: 161.
11. Herrschaft H, Duus P, Gleim F, Ungerheuer E. Preoperative and postoperative cerebral blood flow in patients with carotid artery stenosis. In: Langfitt TW, McHenry LC, Reirich M, Woolman H, eds. *Cerebral Circulation and Metabolism*. New York: Springer Verlag, 1975: 276.
12. Schroeder T, Holstein PE, Engell HC. Hyperperfusion following endarterectomy. *Stroke* 1984; **15**: 758.
13. Diem K, Lentner C. *Documenta Geigy: Scientific tables*. 7th edition. Basle: Geigy, 1970: 61.
14. Barnett HJM, Plum F, Walton JN. Carotid endarterectomy—an expression of concern. *Stroke* 1984; **15**: 941–3.
15. Taylor DW, Sackett DL, Haynes RB. Sample size for randomised trials in stroke prevention. How many Patients do we need? *Stroke* 1984; 15: 968–71.
16. Pickard J, Tamura A, Stewart M, McGeorge A, Fitch W. Prostacyclin, indomethacin and cerebral circulation. *Brain Res* 1980; **197**: 425–31.
17. Browse NL, Ross Russell R. Carotid endarterectomy and the Javid shunt: the early results of 215 consecutive operations for transient ischaemic attacks. *Br J Surg* 1984; **71**: 53–7.
18. Bishop CCR, Insall M, Rutt D, Ross Russell R, Browse NL. The response of carotid and vertebral artery blood flow to hypercapnia: a cerebrovascular stress test. *J Cardiovasc Surg* 1985; **26**(s): 114.
19. Blaumanis OR, Grady PA. Shear stress injury to arterial walls.*Adv Neurol* 1981; **30**: 167–74.

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Long-term effect of carotid endarterectomy on carotid sinus baroreceptor function and blood pressure control

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In order to assess whether carotid endarterectomy had any long-term hypotensive effect, by altering the function of the carotid sinus baroreceptors, blood pressure and carotid sinus baroreceptor function were recorded in 25 patients undergoing carotid endarterectomy. No overall change in blood pressure was recorded 6 months after surgery. Sinus function was shown to decrease in 2 (8 per cent), to remain unchanged in 15 (60 per cent) and to increase in 8 (32 per cent) patients 6 months postoperatively. There was no relationship between changes in sinus function and changes in blood pressure over the 6 months period. Thus, carotid endarterectomy has no long-term hypotensive effect.

Keywords: Carotid sinus, carotid arteries, pressoreceptors

Since the discovery of the carotid sinus reflexes by Hering[1] there has been continuing debate concerning the role of the carotid sinus baroreceptors in the development and maintenance of hypertension[2,3].

Atherosclerotic deposits within the carotid sinus might reduce the distensibility of the sinus consequently reducing afferent carotid sinus nerve (CSN) activity. This might lead to the development of hypertension by an increase in the peripheral vascular resistance[4–9]. Hypotension, immediately after carotid endarterectomy, has been related to changes in the mechanical behaviour of the carotid sinus, brought about by the operative removal of the rigid atheromatous plaques from within that region[10]. The long-term effects of this operation on baroreceptor function and blood pressure are unknown[11].

Patients and method

A total of 25 patients undergoing 28 carotid endarterectomies were studied. The mean age of these patients was 56·3 ± 6·3 years (range 39–66) and the male:female ratio was 21:4. The carotid sinus nerve was preserved during surgery[10].

Blood pressures were measured, at the same time of day, pre-operatively, and at 6 and 26 weeks postoperatively by means of a Bosomat IId automatic blood pressure recorder (Bosch and Sohn, FRG). After 15 min rest in the supine position in a quiet laboratory, six recordings were taken at 1 min intervals. The mean values of the last three systolic and last three diastolic pressures were those used. Mean arterial blood pressure (MABP) was calculated as being the diastolic pressure plus one-third of the pulse pressure. The instrument was regularly calibrated against a mercury sphygmomanometer throughout the period of study. Those patients with a blood pressure of $>140/90$ mmHg were classified as being hypertensive.

Assessment of carotid sinus baroreceptor function was made by means of neck suction[12,13] pre-operatively and 6 months postoperatively. Neck suction reduces the intracervical tissue pressure, thus increasing the carotid sinus transmural pressure, resulting in a reflex bradycardia and a fall in blood pressure[13].

The neck chamber followed the design of Eckberg *et al.*[13]. Recordings were made in the fasting state, after micturition and were taken in the supine position. Heart interval (R–R interval, ms) was measured from a continuously recording 4-limb ECG. Neck suction was applied for five heart beats, at levels from -10 to -50 mmHg, in 10 mmHg decrements (*Figure 1*). Three recordings were made at each level of suction; the latter was measured by a transducer (Bell and Howell, 4-327-1) mounted directly onto the neck chamber.

Respiratory movements were recorded by a stethograph and transducer. ECG, respiratory and neck chamber pressure signals were amplified (Roche, 211-1, 224-1) and were recorded onto electromagnetic tape (Racal), at a speed of $1\frac{7}{8}$ in. s^{-1} for later computer analysis. To minimize the effect of sinus arrhythmia on the base line pulse interval all recordings were undertaken during held expiration.

The mean of the three R–R intervals preceeding the onset of neck suction was subtracted from the maximum R–R interval recorded during stimulation to give the maximum R–R interval prolongation (Δ R–R). At each level of suction these values (Δ R–R) were plotted against the level of suction used. Using the method of least squares a linear regression line was drawn and the gradient of this line gave an index of the sensitivity (gain) of the carotid sinus baroreceptors (CSBS) expressed in ms mmHg^{-1}. Only regression lines with $r > 0·75$ and $P < 0·05$ were used.

Statistical method

The blood pressure results were compared by means of Student's *t* test for unpaired data. In a separate study of 18 normal volunteers (T. C. B. Dehn and J. E. Angell-James, unpublished data) it was found that the 95 per cent confidence interval of the mean difference of CSBS, between two separate assessments in the same individual, was 3·67 ms mmHg^{-1}. After carotid endarterectomy, changes in the calculated CSBS of less than this figure were, therefore, treated as being physiologically insignificant.

Ethical committee approval

The investigation was approved by the Ethical Committee of the hospital. Consent was obtained from all the patients undergoing this study.

Results

The results of the values of the carotid sinus baroreceptor sensitivity are illustrated in *Figure 2* and *Table 1*. The mean pre-operative CSBS was 3·42 ± 0·49 ms mmHg^{-1} and 5·24 ± 1·04 ms mmHg^{-1} when recorded 6 months postoperatively. No physiologically significant changes in the CSBS were recorded postoperatively in 15 patients; in 2 patients decreases in the CSBS were measured postoperatively. Both the latter patients underwent bilateral surgery; the decreases in the CSBS were recorded after the first operation and the results were unchanged following surgery to the contralateral side. In eight patients an increase of CSBS was recorded 6 months postoperatively. The mean increase in these patients was 7·47 ± 1·17 ms mmHg^{-1} and the maximum increase recorded was 18·5 ms mmHg^{-1}. In one patient of the latter group the increase in CSBS was recorded following the second-side operation.

The results of the blood pressure measurements are shown in *Table 2*. There was no overall change in the MABP

Parts of this work have been presented to the Vascular Surgical Society, the Surgical Research Society, the Medical Research Society and the Physiological Society. This work forms part of the MS Thesis (London) of T. C. B. Dehn

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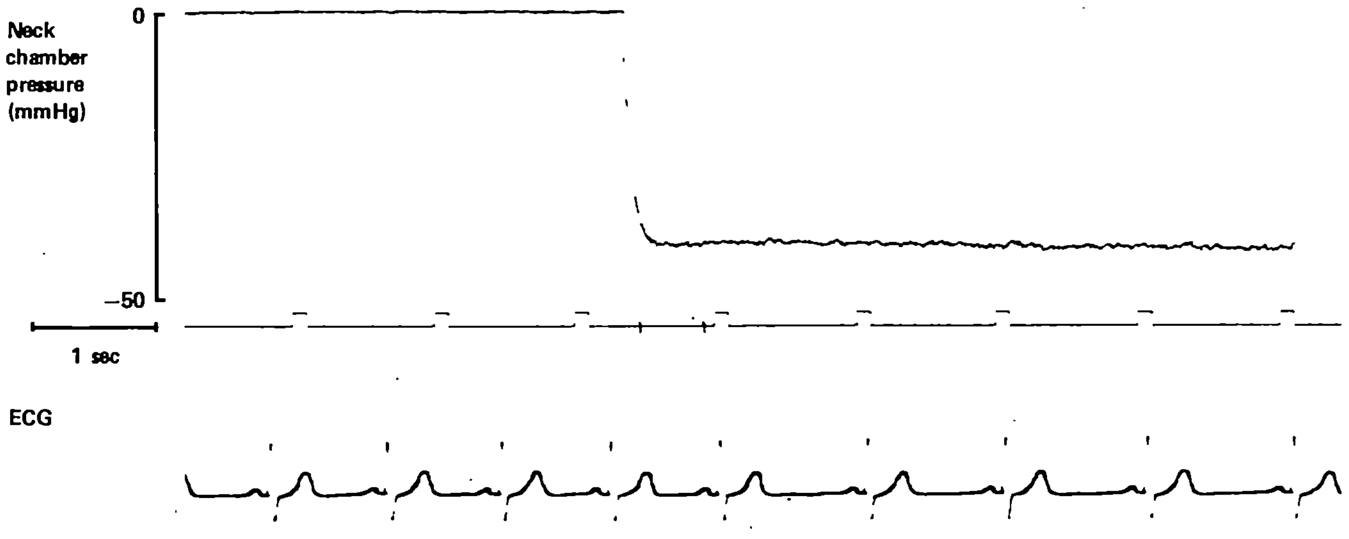

Figure 1 *Original recording of neck suction test, at −40 mmHg, recorded from a patient 6 months after unilateral carotid endarterectomy*

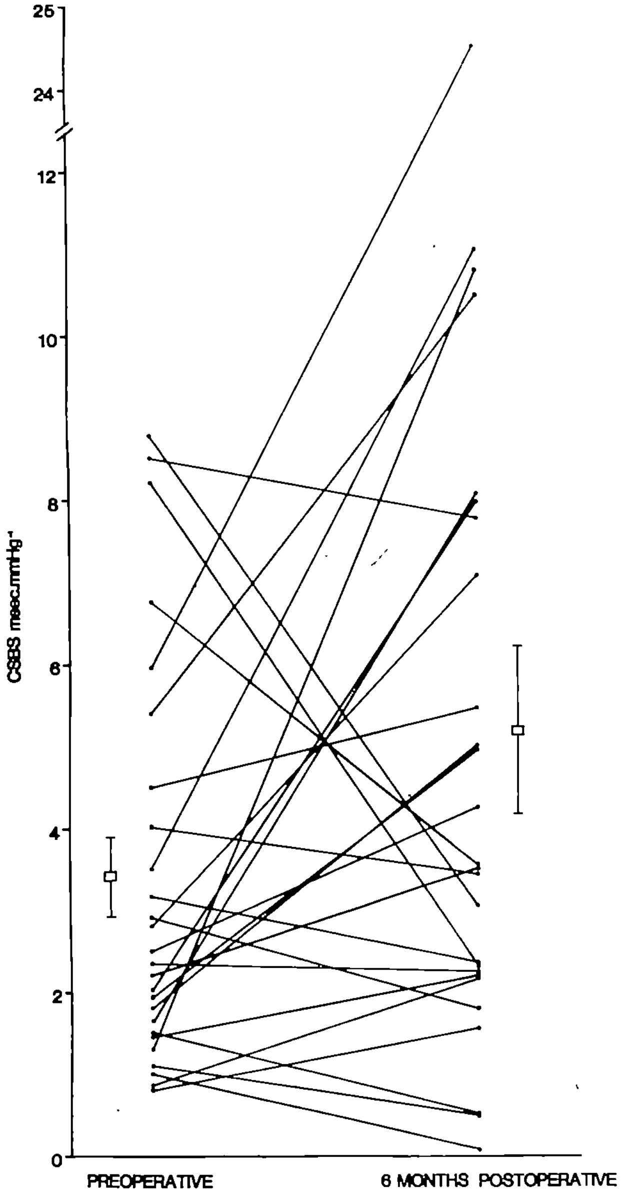

Figure 2 *Results of the carotid sinus baroreceptor sensitivities in 25 patients before, and 6 months after carotid endarterectomy (—□—, mean±s.e.m.)*

Table 1 *Results of carotid sinus baroreceptor sensitivity before and after operation measured in 25 patients undergoing carotid endarterectomy*

	Pre-operative	Postoperative	Mean values of individual differences between pre-operative and postoperative results
No change $(n=15)$	2·92±0·57	2·72±0·57	−0·38±0·35
Decrease $(n=2)$	8·49±0·29	3·05±0·36	−5·81±0·07
Increase $(n=8)$	3·07±0·62	10·58±2·10	+7·47±1·17
Whole group $(n=25)$	3·42±0·49	5·24±1·04	+1·89±0·60

Results are expressed as mean±s.e.m. (ms mmHg^{-1})

Table 2 *Blood pressure measurements recorded before and at two intervals after operation in 25 patients undergoing carotid endarterectomy*

	Pre-operative	6 weeks postoperative	6 months postoperative
Systolic blood pressure	149·0±4·9	149·8±6·0	148·7±4·4
Diastolic blood pressure	88·2±2·5	87·8±2·6	88·5±2·5
Mean blood pressure	108·5±3·0	108·5±3·4	108·6±2·3

Results are expressed as mean±s.e.m. (mmHg)

postoperatively. There was a slight, but insignificant, fall in the systolic and the MABP of the 16 pre-operatively hypertensive patients (*Table 3*). Six months postoperatively, the MABP had increased by >10 mmHg in three patients ($\bar{x}=20$ mmHg), had decreased by >10 mmHg in six patients ($\bar{x}=11{\cdot}7$ mmHg) and had remained within ± 10 mmHg of the pre-operative value in the remaining seven patients of this group.

The lack of consistent relationship between the changes in the CSBS and the changes in the MABP between the pre-operative and 6 month postoperative values is illustrated in *Figure 3*.

Discussion

The carotid sinus baroreceptors are stimulated by the distension of the vessel wall which occurs with the normal pulse pressure

Table 3 *Blood pressure measurements recorded in 16 pre-operatively hypertensive patients undergoing carotid endarterectomy*

	Pre-operative	6 weeks postoperative	6 months postoperative
Systolic blood pressure	160·7±5·7	159·1±8·1	153·8±5·5
Diastolic blood pressure	93·9±2·9	91·4±3·4	92·0±3·1
Mean blood pressure	116·0±3·3	113·8±4·5	112·6±2·7

Results are expressed as mean±s.e.m. (mmHg)

wave[14]. Distensibility of the vessel wall is reduced by atherosclerosis, both in the human carotid sinus[8] and the aorta of the experimental atheromatous animal[7]. Furthermore, in atherosclerosis the baroreceptors are known not only to be reset to operate at a higher threshold pressure, but also to have a reduced sensitivity[6,9,15,16].

Atherosclerosis particularly affects the carotid sinus region[17] and, although hypertension commonly is found amongst atherosclerotic patients[18], the relationship is uncertain between the extent of atherosclerosis at this site and the degree of hypertension[19,20]. Carotid sinus atherosclerosis may result in the occurrence of transient ischaemic attacks, a condition now treated frequently by the operation of carotid endarterectomy.

Hypotension and bradycardia may occur in up to 50 per cent of patients in the first 24 h following carotid endarterectomy[10,21–24]: these circulatory changes have been attributed to the effects of excising the rigid atheromatous plaque from the carotid sinus, thus improving the function of the baroreceptors situated therein[10,21]. Temporary reversal of these early postoperative changes can be effected by the infiltration of local anaesthetic solution alongside the carotid sinus nerve (CSN), thus illustrating their reflex nature[10,23,24].

Baroreceptor-mediated hypotension after carotid endarterectomy will, however, only be observed when the CSN is carefully preserved at surgery[10,23,24] and does not complicate endarterectomies in which this nerve is divided.

Angell-James and Lumley[10] studied the mechanical changes in the carotid sinus, whilst simultaneously recording the CSN activity, in 11 patients undergoing carotid endarterectomy. They reported an inverse relationship between the postendarterectomy CSN activity and the systemic blood pressure. Surprisingly, they found that the distensibility of the carotid sinus was reduced immediately postoperatively, although the end diastolic diameter increased in seven patients. In six cases they reported a direct relationship between CSN activity and carotid sinus diameter after surgery.

The present study is the first to report the long-term effects of this operation on both carotid sinus baroreceptor function and blood pressure. Local pathological changes, arising postoperatively, may effect carotid sinus baroreceptor function. Endarterectomy results in oedema of the vessel wall[25,26]; both this and the resolution of cervical haematoma may result in periarterial fibrosis, thus diminishing sinus wall distensibility. Additionally, inadvertent operative trauma to the carotid sinus baroreceptors or carotid sinus nerve may occur[10]; these factors would explain the decreases in CSBS which were recorded in 2 patients.

The postoperative values of CSBS in the eight patients in whom the CSBS increased were similar to those recorded in a group with the carotid sinus syndrome[27]. Several factors may contribute towards an increase in the CSBS following carotid endarterectomy. Firstly, the act of endarterectomy may increase the number of functioning baroreceptor units. Secondly, endarterectomy would increase the radius between the centre of the sinus and the adventitial baroreceptors thus, by the law of Laplace, increasing circumferential wall tension and baroreceptor discharge. Finally, by altering the mechanical properties of the sinus wall the operating range of the baroreceptors may be shifted, to be within the steep linear portion of the sigmoid shaped stimulus/response curve where maximum fibre recruitment and sensitivity occur[2].

In 60 per cent of the patients studied no significant changes were recorded in the CSBS after carotid endarterectomy. This may arise because, in some of this group, no permanent alterations were maintained postoperatively in the visco-elastic properties of the endarterectomized sinus. Alternatively, the endarterectomy may have resulted in such dilatation of the sinus that further expansion, secondary to an increase in transmural pressure, would be limited by adventitial collagen fibres[10]. Changes in transmural pressure at maximum vessel diameter cause little, if any, change in baroreceptor discharge[28].

Our results demonstrate that, after carotid endarterectomy, there is no overall long-term reduction in blood pressure. Thus, any effect that endarterectomy might have on the carotid sinus baroreceptor control of blood pressure is of short duration. This may occur either because of baroreceptor adaptation or because central mechanisms controlling the reflex arc may 'filter' the afferent information from the operated side, in a similar manner to that which has been postulated to occur during unilateral carotid sinus nerve stimulation[29]. Tyden *et al.*[30], using neck suction, recorded both blood pressure and carotid sinus baroreceptor function in eight patients before and after carotid endarterectomy. Postoperatively they recorded a mean increase in MABP of 14 mmHg, but the closed-loop gain of the carotid baroreceptors was the same as that recorded pre-operatively. Their recordings were made 8 weeks postoperatively, a time at which subcutaneous induration may still persist. This may reduce the transmission of neck suction to the carotid sinus and, since only one level of suction (−40 mmHg) was employed, the value of comparison of the two sets of their results may be reduced.

The lack of relationship between changes in CSBS and MABP after carotid endarterectomy might be accounted for by the lability of blood pressure commonly found amongst elderly atherosclerotic patients[31]. Moreover, patients with a hypersensitive carotid sinus reflex, such as may occur in the carotid sinus syndrome, do not suffer from persistently low blood pressures and frequently are found to be hypertensive[32]. Some similarities may be drawn between patients with this syndrome and those in whom the CSBS increased after carotid endarterectomy, since in both groups it is common to find only one hypersensitive sinus. The increase in afferent nerve activity arising from that sinus does not appear to effect a change in the basal level of the blood pressure.

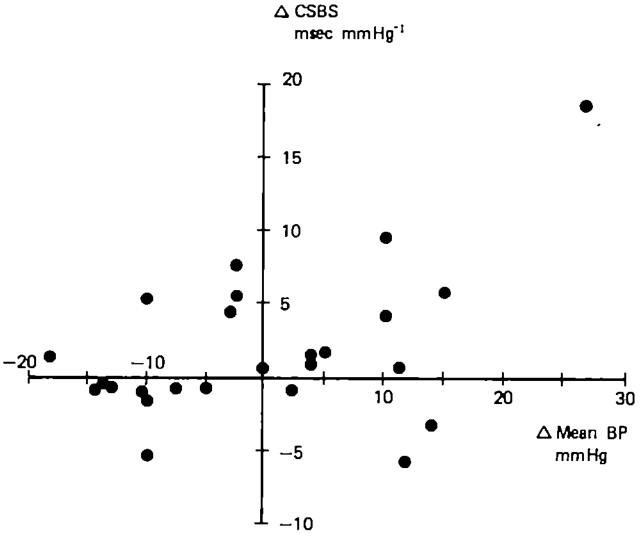

Figure 3 *Scatter diagram illustrating the changes in carotid sinus baroreceptor sensitivity and mean blood pressure over 6 months in 25 patients undergoing carotid endarterectomy*

Although carotid endarterectomy may increase the sensitivity of the carotid sinus baroreceptors in a proportion of patients, this operation, by virtue of its effect on the sinus baroreceptors, has no long-term antihypertensive properties. This further implies that carotid sinus baroreceptors are only one part of the multifactorial control of blood pressure.

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References

1. Hering HE. Der Karotisdruckeursch. *Munch Med Wschr* 1923; **70**: 1287–90.
2. Heymans C, Neil E. In: *Reflexogenic Areas of the Cardiovascular System*. London: Churchill, 1958.
3. Sleight P. Reflex control of the heart. *Am J Cardiol* 1979; **44**: 889–94.
4. Hering HE. Die Karotissinus reflexe auf Hers und Gefasse. Leipzig: Steinkopff, 1927.
5. Horrobin DF. A theory of hypertension. *Lancet* 1966; **i**: 574–79.
6. Angell-James JE. Arterial baroreceptor activity in rabbits with experimental atherosclerosis. *Circ Res* 1974; **34**: 27–39.
7. Winson M, Heath D, Smith P. Extensibility of the human carotid sinus. *Cardiovasc Res* 1974; **8**: 58–64.
8. Sleight P. Neurophysiology of the carotid sinus receptors in normal and hypertensive animals and man. *Cardiology* 1976; **61** (Suppl 1): 31–45.
9. Cox RH, Bagshaw RJ, Detweiler DK. Alterations in carotid sinus reflex control of arterial haemodynamics associated with experimental hyperlipidemia in the racing greyhound. *Circ Res* 1980; **46**: 237–44.
10. Angell-James JE, Lumley, JSP. The effects of carotid endarterectomy on the mechanical properties of the carotid sinus and carotid sinus nerve activity in atherosclerotic patients. *Br J Surg* 1974; **61**: 305–10.
11. Baroreceptors and high blood pressure. Editorial. *Lancet* 1979; **i**: 1277–9.
12. Ernsting J, Parry DJ. Some observations on the effects of stimulating the stretch receptors in the carotid artery of man. *J Physiol* 1957; **137**: 45p.
13. Eckberg DL, Cavanaugh MS, Mark AL *et al.* A simplified neck suction device for activation of carotid baroreceptors. *J Lab Clin Med* 1975; **85**: 167–73.
14. Hauss WH, Kreuziger H, Asteroth H. Uber die Riezung der Pressorezeptoren in sinus caroticus beim hund. *Kreisl-forsch* 1949; **38**: 28–33.
15. Randall OS, Esler MD, Bulloch GF *et al.* Relationship of age and blood pressure to baroreflex sensitivity and arterial compliance in man. *Cli Sci Mol Med* 1976; **51**: 357–60S.
16. Vlachakis ND, Mendlowitz M, De Gusman D DeG. Diminished baroreceptor sensitivity of elderly hypertensives. Possible role of atherosclerosis. *Atherosclerosis* 1976; **24**: 243–9.
17. Heath D, Smith P, Harris P *et al.* The atherosclerotic human carotid sinus. *J Path Bact* 1973; **110**: 49–58.
18. de Bono DP, Warlow CP. Potential sources of emboli in patients with presumed transient cerebral or retinal ischaemia. *Lancet* 1981; **i**: 343–5.
19. Hasselbach HV. Besthen Bezieuhungen zwischen veranderungen am sinus caroticus und der hypertonie. *Allgem Path.* 1931; **86**: 369–74.
20. Evans PH. Relation of longstanding blood pressure levels to atherosclerosis. *Lancet* 1965; **i**: 516–19.
21. Tarlov E, Schmidek H, Scott RH *et al.* Reflex hypotension following carotid endarterectomy. *J Neurosurg* 1973; **39**: 323–7.
22. Bove EL, Fry WJ, Gross WS *et al.* Hypotension and hypertension as consequence of baroreceptor dysfunction following carotid endarterectomy. *Surgery* 1978; **85**: 633–7.
23. Tyden, G, Samnegard H, Thulin L. Rational treatment of hypotension after carotid endarterectomy by carotid sinus nerve blockade. *Acta Chir Scand* 1980; **500** (Suppl): 61–4.
24. Cafferata HT, Merchant RF, De Palma RG. Avoidance of postcarotid endarterectomy hypertension. *Ann Surg* 1982; **196**: 465–72.
25. French BN, Rewcastle NB. Sequential morphological changes at the site of carotid endarterectomy. *J Neurosurg* 1974; **41**: 745–54.
26. Dirrenbeiger RA, Sundt TM. Carotid endarterectomy. Temporal profile of the healing process and effects of anticoagulation therapy. *J Neurosurg* 1978; **48**: 201–19.
27. Dehn TCB, Morley CA, Sutton R. A scientific evaluation of the carotid sinus syndrome. *Cardiovasc Res* 1984; **18**: 746–51.
28. Bergel DH, Bertram CD, Brooks DE *et al.* Simultaneous recording of the carotid sinus dimensions and the baroreceptor nerve in the anaesthetised dog. *J Physiol* 1975; **252**: 15–16P.
29. Griffith LSC, Schwartz SI. Reversal of renal hypertension by electrical stimulation of the carotid sinus nerve. *Surgery* 1964; **56**: 232–9.
30. Tyden G, Samnegard H, Melcher A *et al.* The effect of carotid endarterectomy on the antihypertensive properties of the carotid sinus reflex. *Acta Chir Scand* 1981; **147**: 15–17.
31. Mancia G, Ferrari A, Gregorini L *et al.* Blood pressure variability in man: its relation to high blood pressure, age and baroreflex sensitivity. *Clin Sci* 1980; **59**: 401–4S.
32. Weiss S, Baker JP. The carotid sinus reflex in health and disease: its role in the causation of fainting and convulsions. *Medicine* 1933; **12**: 297–354.

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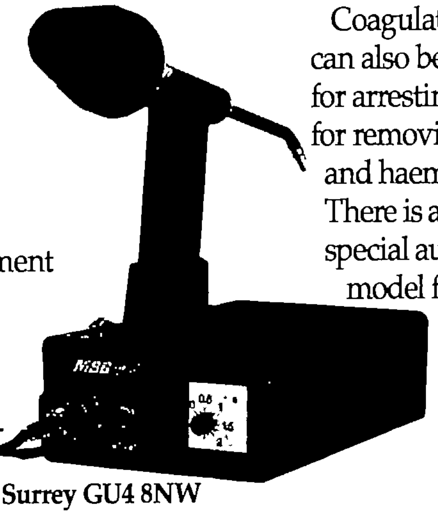

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Subclavian vascular injuries

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This study comprises 228 patients with penetrating injuries of the subclavian vessels. The vein alone was involved in 44 per cent, the artery alone in 39 per cent, and both vessels in 17 per cent. The majority of the victims (61 per cent) did not reach the hospital alive, and in those who were operated on the mortality was 15·5 per cent (overall mortality 66 per cent). The overall mortality of venous injuries was significantly higher than the arterial ones ($P<0{\cdot}01$)*, probably because of the dangerous complication of air embolism. Physical examination is reliable in the diagnosis of these injuries and there is no need for an emergency angiogram. The clavicular incision was the preferred approach. Repair was performed in 94 per cent of those with arterial injury. Vein injuries were treated by suture in 60 per cent and ligation in 40 per cent. A selective conservative approach is advised.*

Keywords: Subclavian, injury, management

Subclavian vessel injuries are rare. Most publications report experience with less than 30 patients. The largest series, 93 patients over a period of 21 years, was reported by Graham *et al.*[1]; Rich *et al.*[2] reported an incidence of less than 1 per cent of subclavian artery injuries in 1000 major vascular injuries. The limited experience of most surgeons with this type of trauma and the difficult exposure and vascular control necessary for their management make subclavian vessel injuries a surgical challenge. The reported mortality varies from 5 per cent to 30 per cent. However, these figures do not represent the real mortality because they refer to a selected group of patients who survived long enough to reach medical care.

Patients and methods

This was a combined retrospective and prospective study over a period of 4 years (1982–1985). During this period 228 patients with subclavian vessel injuries were seen at Baragwanath Hospital, Johannesburg. Most of them (138 or 61 per cent) were certified dead on arrival and were transferred to the mortuary. The remaining 90 (39 per cent) received surgical treatment. Data concerning the first group of patients was obtained from the mortuary records.

Most of the patients were males (93 per cent) and their age ranged between 14 and 66 years (mean 26). The wound was inflicted by a knife in the majority of the patients (98 per cent).

Management

Patients with no sign of life when seen by the Casualty Officer were sent straight to the mortuary without attempted resuscitation. However, patients who arrested after admission to the hospital were resuscitated: an endotracheal tube was inserted, fluids were infused, and a thoracotomy was performed, with the patient on the stretcher and without any aseptic precautions. The bleeding was controlled, the aorta was cross-clamped, and cardiac resuscitation was carried out by means of massage, transfusions, $CaCl_2$, $NaHCO_3$, adrenaline and defibrillation as required. The right ventricle of the heart was directly aspirated for air embolism. If the heart recovered, the operation was completed in the operating theatre.

Patients presenting with active bleeding from the wound had external compression applied to the wound to control bleeding, and were put in the Trendelenburg position. These simple manoeuvres decrease the risk of air embolism which is a common cause of death in injuries of major neck veins. One or more large bore intravenous cannulae were inserted, always contralateral to the side of injury to avoid extravasation of the infused fluids from a proximal venous injury. In exsanguinated patients, O Rh-negative low titre unmatched blood was administered. Any associated pneumothorax, however minor, was drained. This is of great importance because an undrained pneumothorax may be converted to a tension pneumothorax when the patient is put on a ventilator and positive pressure applied.

The physical examination included assessment of the haemodynamic status, of pulses distal to the injury, and function of the brachial plexus and of the sympathetic chain (Horner's syndrome). The patient was examined for a bruit, an expanding or pulsatile haematoma, blood in the sputum, painful swallowing and subcutaneous emphysema. Erect chest and neck X-rays were done on all stable patients, and checked for pneumothorax, mediastinal or subcutaneous emphysema, and widened upper mediastinum. A widened mediastinum was managed either by operation if the patient was shocked or further assessed by an aortic arch angiogram in haemodynamically stable patients. The incision of choice was a clavicular one with or without excision of the medial half of the clavicle, or clavicular division lateral to the insertion of the sternomastoid muscles, or dislocation of the sternoclavicular joint. In proximal injuries the clavicular incision may be combined with a median sternotomy.

Results

Initial clinical assessment

Most of the patients were certified dead on arrival at the hospital (138 patients or 61 per cent). In the remaining 90 patients (39 per cent) who reached the hospital alive the most common finding was shock (72 per cent). In 22 per cent of the victims the blood pressure was unrecordable. Active bleeding from the wound was recorded in 65 per cent of the patients, an absent or diminished peripheral pulse in 33 per cent, an expanding neck haematoma in 20 per cent, and a bruit in 18 per cent.

Twelve patients (13 per cent) were admitted to hospital electively or semi-electively for post-traumatic aneurysms or arteriovenous fistula. Most of these patients had been referred from peripheral hospitals. Emergency angiograms were performed on only three patients, who had a widened mediastinum on the chest X-ray and were haemodynamically stable. The angiogram was normal in all three cases.

Operative approach

In the majority of the patients (71 per cent) a clavicular incision with or without resection of the medial half of the clavicle or dislocation of the sternoclavicular joint provided adequate exposure. In 27 per cent the clavicular incision was combined with a median sternotomy, and in 2 per cent a 'trap door' was employed. In 58 of the 62 patients (94 per cent) with subclavian artery injury the continuity of the vessels was restored by a simple repair or an end-to-end anastomosis (34 cases) or by means of a graft (autologous vein in 19, polytetrafluoroethylene, in 5). In four moribund patients arterial ligation was performed. Most venous injuries (60 per cent) were repaired by suturing, while in the remaining 40 per cent a ligation was done.

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Injured structures

In the majority of patients (74 per cent) the wound was located in the left side of the neck, the majority of assailants being right-handed. The subclavian artery alone was injured in 89 patients (39 per cent), the subclavian vein alone in 101 patients (44 per cent), and both vessels in 38 patients (17 per cent). The most commonly found associated injury was a haemopneumothorax (55 per cent) followed by a brachial plexus injury (14 per cent), and another major vessel injury (e.g. carotid, jugular etc.) in 10 per cent.

Mortality and morbidity

The overall mortality was 66 per cent. The operative mortality was 15·5 per cent. Of the 14 operative deaths 6 occurred in theatre and the remaining 8 within hours or days of the operation. All 14 patients were admitted in severe shock, the blood pressure being unrecordable in 8 of them. Air embolism was confirmed as the cause of death in at least three patients with venous injuries.

Venous injuries had significantly higher mortality than arterial injuries. Although the operative mortality was similar (21 per cent and 18 per cent respectively, χ^2 test $P > 0{\cdot}05$), the overall mortality was 82 per cent and 60 per cent respectively ($P < 0{\cdot}01$). Both arterial and venous injuries groups were similar with regard to age, sex, weapon and associated injuries.

There were 14 major postoperative complications in the 76 survivors (18 per cent). These included eight cases of pneumonia, two of brain damage, two occluded grafts, one case of secondary bleeding from a venous graft site, and one of wound sepsis.

Discussion

The management of penetrating neck injuries is a controversial issue. Many authors advocate routine exploration on every patient where the platysma has been penetrated. Others apply various forms of selective conservatism. At Baragwanath Hospital we have been practising a policy of selective conservatism for many years and we believe that it is safe[3]. A careful physical examination is reliable in identifying injuries requiring surgical exploration. Physical signs suggestive of significant vascular injury are active bleeding, an expanding or pulsatile haematoma, an absent or diminished peripheral pulse, and a bruit[3]. The presence of shock responding to a small amount of fluids is not an absolute indication for operation. By following these criteria our incidence of delayed diagnosis of vascular injuries (false aneurysm, arteriovenous fistulae) was less than 2 per cent of the conservatively managed patients[3].

It has been suggested that arteriography should be performed on all stable patients with wounds in the supraclavicular region[4,5]. We believe that the value of the emergency angiogram in these patients is limited, and we reserve this investigation only for stable patients whose chest X-ray shows a widened mediastinum. The proponents of this diagnostic procedure suggest that it may help in selecting the patients requiring surgery and in planning the optimal incision pre-operatively. However, in our experience the decision to operate or not can safely be taken exclusively on clinical criteria[3]. Furthermore an arteriogram is often falsely negative[6] and venous injuries may be missed. With reference to the planning of the incision we believe that this can be done accurately without the help of an arteriogram. All patients with wounds at the base of the neck should have the chest area prepared for a possible median sternotomy in addition to the standard clavicular incision. A cautious digital exploration of the wound will give information about the direction of the knife tract, i.e. towards or away from the proximal or distal subclavian vessels. This information will help determine whether the patient needs further exposure by means of a median sternotomy.

Familiarity with the anatomy of the region is important in the management of subclavian vessels injury. The incision of choice is a clavicular one which starts at the sternoclavicular junction, then passes along the medial half of the clavicle and then curves downwards towards the deltopectoral groove. The medial half of the clavicle is resected or the sternoclavicular joint is disarticulated. Subperiosteal partial excision of the clavicle does not lead to deformity or dysfunction. Complete regeneration takes place in 6–8 weeks[7]. There has been criticism of the clavicular resection or dislocation as time-consuming with insignificant additional exposure[1]. However, the suggested alternative of 'book' thoracotomy or 'trap door' is more time-consuming, is associated with excessive bleeding, iatrogenic rib fractures are a common problem, and the incidence of postoperative pulmonary complications is high.

Many authors recommend a standard left thoracotomy or a small left anterior thoracotomy in the second or third intercostal space for injuries involving the proximal left subclavian artery[8,9]. For all proximal injuries, irrespective of side, we use the clavicular incision combined with a median sternotomy. The exposure is satisfactory and the problems associated with a thoracotomy are avoided.

Arterial injuries are best managed by a simple repair or debridement and an end-to-end anastomosis. If an interposition graft is necessary an autologous vein is generally considered to be the material of choice, although we did not record any problems in the five cases where a synthetic graft was used. Feliciano *et al.*[10] showed that synthetic grafts in vascular trauma are safe and there is no increased danger of sepsis. Schimpf *et al.*[11] showed in autopsy studies that primary anastomosis can almost always be achieved by mobilizing and passing the axillary artery through the first intercostal space. With this technique, up to 7·5 cm of the subclavian artery can be resected and primary anastomosis achieved. Ligation of the subclavian artery should be avoided whenever possible. Claudication of the arm may occur, and if the ligation is proximal to the vertebral artery there is the possibility of the subclavian steal syndrome developing. It is preferable to repair subclavian vein injuries but if there are any technical problems ligation can be performed without any serious consequences. Any associated brachial plexus injuries are primarily repaired.

The reported mortality for subclavian vessel injuries varies between 5 per cent and 30 per cent[1,4]. However, these findings refer to a small series of patients over a long period of time, and do not include the patients who never reached the hospital alive. Our operative mortality was 15·5 per cent, but the overall mortality was 66 per cent. Although the operative mortality for arterial and venous injuries was similar, the overall mortality of venous injuries was significantly higher than the arterial ones (82 per cent *versus* 60 per cent, $P < 0{\cdot}01$). The worse prognosis of the venous injuries is most probably due to the fatal complication of air embolism. The importance of preventing this problem by direct compression over the wound and positioning the patient in the Trendelenburg position cannot be overemphasized. If the patient arrests a resuscitative thoracotomy should be performed and the heart should be aspirated for air[12].

References

1. Graham J, Feliciano D, Mattox K, Beall A, Debakey M. Management of subclavian vascular injuries. *J Trauma* 1980; **20**: 537–44.
2. Rich NM, Baugh JH, Hughes C. Acute arterial injuries in Vietnam: 1000 cases. *J Trauma* 1970; **10**: 359–69.
3. Demetriades D, Stewart M. Penetrating injuries of the neck. *Ann R Coll Surg Engl* 1985; **67**: 71–4.
4. Lim L, Saletta J, Flanigan D. Subclavian and innominate artery trauma. *Surgery* 1979; **86**: 890–7.
5. Sankaran S, Walt A. Penetrating wounds of the neck: principles and some controversies. *Surg Clin N Am* 1977; **57**: 139–50.
6. Perry M, Thal E, Shires E. Management of arterial injuries. *Ann Surg* 1971; **173**: 403–8.
7. Old W, Oswaks R. Clavicular excision in management of vascular trauma. *Am Surg* 1984; **50**: 286–9.

8. Zelenock G, Kazmers A, Graham L, Erlandson E, Cronenwett J, Whitehouse N *et al*. Non penetrating subclavian artery injuries. *Arch Surg* 1985; **120**: 685–92.
9. Sturn J, Dorsey J, Olson F, Perry J. The management of subclavian artery injuries following blunt thoracic trauma. *Ann Thorac Surg* 1984; **38**: 188–91.
10. Feliciano D, Mattox K, Graham J, Bitondo C. Five-year experience with PTFE grafts in vascular wounds. *J Trauma* 1985; **25**: 71–82.
11. Schimpf P, Burt D, Wagner R. Left subclavian artery trauma: in situ vs rib interspace mobilisation for primary anastomosis. *J Trauma* 1985; 25: 1069–73.
12. Demetriades D, Rabinowitz B, Sofianos C. Emergency room thoracotomy for stab wounds to the chest and neck. *J Trauma* 1987; **27**: 483–5.

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Surgical workshop

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Internal jugular vein cannulation: refinements of technique for long-term parenteral therapy

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Unanimity is lacking on the best technique for long-term venous access in patients on supplemental or total intravenous nutrition. Probably for simplicity, straightforward percutaneous subclavian insertion is most satisfactory but it does carry a risk of pneumothorax and arterial puncture. Direct exposure and cannulation of a large vein in the neck reduces these risks. The external jugular vein is favoured by some surgeons but cannot be cannulated in 10–20 per cent of cases. For these reasons we have developed the direct exposure technique for the subclavian or internal jugular vein, which, with experience, is no more difficult than cannulating the external jugular vein. Tunnelling the catheter back from the neck is desirable to try to reduce the possibility of sepsis and is essential for easy access to the connector on the chest wall, and to avoid the nuisance, for both patient and attendants, of a line emerging in the neck. Integrally moulded multilumen catheters are becoming more common in our practice, particularly when an additional portal is required for large volumes of crystalloid replacement in patients with high output fistulae or prolonged adhesive obstruction. These cannot be tunnelled retrograde after insertion into the vein.

Technique

The patient is positioned supine, on an X-ray table with the neck extended and rotated away from the side of insertion. The head is supported on a ring. After skin preparation and draping, local anaesthetic is infiltrated. The incision is made 1 cm superior to the medial end of the clavicle. The internal jugular vein is exposed between the two heads of sternocleidomastoid and slung between tapes. A 5-0 Prolene* purse string is inserted at the site of proposed puncture.

The subcutaneous tunnel begins above the site of puncture and emerges at a level between the third and fourth ribs on the contralateral side. It passes through the subcutaneous tissues by way of the suprasternal notch and through the deep fibres of the sternal head of sternocleidomastoid. The catheter is introduced prograde with either a Redivac (OEC Orthopaedic) introducer, threaded on the end of the catheter (*Figure 1*) or via a cannula previously introduced (*Figure 2*) depending on the type of catheter being used. The vein is then cannulated by direct puncture. The position of the catheter tip is checked with the image intensifier. The two heads of sternocleidomastoid are approximated with interrupted absorbable sutures and the skin closed with interrupted sutures.

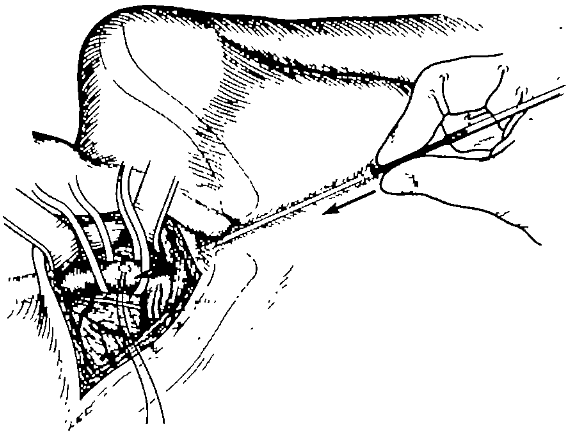

Figure 1 *Prograde insertion of catheter with Redivac introducer*

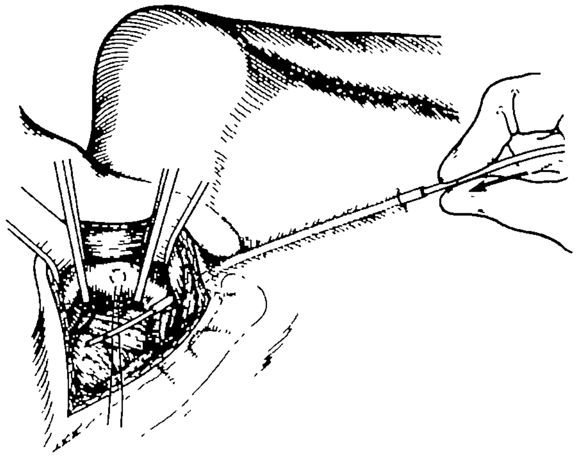

Figure 2 *Insertion via previously introduced cannula*

Direct tunnelling brings the line across the clavicle where it not only makes an unsightly bulge but, in a thin patient, can result in erosion of the overlying skin. Direct tunnelling also results in the catheter lying directly beneath the wound in the neck and, at least in theory, increases the risk of catheter sepsis if a superficial wound infection should occur. Less flexible polyurethane catheters may also kink if angled across bone. For these reasons we now routinely tunnel medially from the neck to the contralateral anterior chest wall via the suprasternal notch making sure that the catheter is taken through the sternal head of sternocleidomastoid. This enables closure of the deep muscle layer and thus excludes the catheter from the superficial part of the wound.

Acknowledgements

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Transluminal angioplasty versus conventional operation in the treatment of haemodialysis fistula stenosis: results from a 5-year study

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In this retrospective study we have used life table analysis to compare the results of 37 transluminal angioplasties with those of 37 conventional operations (thrombectomy, thrombendarterectomy with/without grafting, bypass) in the treatment of stenoses and occlusions of haemodialysis fistulae. There was no difference between the groups in terms of lesion morphology or the patients' age and sex. Cumulative patency rates for angioplasty and surgery, respectively, were 94·5 and 78·1 per cent after 1 week, 72·3 and 64·1 per cent after 1 month, 41·2 and 28·9 per cent after 5 months and 31·3 and 19·3 per cent after 1 year (χ^2 test, $P<0·001$). The difference is due mainly to a high percentage of early occlusions in the first week after surgery. When transluminal angioplasty of haemodialysis fistula stenoses is possible it achieves results which are at least as good as those of operation.

Keywords: Transluminal angioplasty, haemodialysis fistula stenosis

Transluminal angioplasty (TA), first described by Dotter[1,2], is now a generally accepted method of treatment of selected forms of arterial occlusive disease[3–5]. Percutaneous or intra-operative transluminal angioplasty has also achieved good results in treating stenoses of arteriovenous haemodialysis fistulae[6]. Infections, stenoses at the site of puncture, aneurysms, and stenoses of the afferent and efferent vessels mean that these fistulae have a limited duration of function and repeated re-interventions are necessary[7,8]. In our patients we found an average number of 0·4 revisions during the whole time of function of the arteriovenous Brescia–Cimino fistula, and of 2·1 revisions for the polytetrafluoroethylene (PTFE) fistula[9]. Until some years ago the generally used treatment of fistula stenosis consisted of operative revision with thrombectomy and grafting, or the construction of bypasses[10]. This non-randomized and retrospective review compares the value of TA with that of conventional surgical methods of treating arteriovenous fistula stenosis.

Patients and methods

Group 1 (dilatations)

From 1981 to 1985 we performed 37 TAs in 22 patients. A total of 23 of the procedures were done percutaneously and 14 intra-operatively. Percutaneous access was preferred in cases of fistula stenosis, while open intra-operative angioplasty was used in cases of fistula occlusion after thrombectomy or angiographic evaluation of possible stenoses. The stenotic lesions were found near or at the site of anastomoses between artery and vein (Brescia–Cimino fistula), between two veins after venous interposition, or between PTFE prosthesis and vein. Stenoses of the efferent vein were dilated whereas those within a PTFE prosthesis had to be operated upon because of the lack of elasticity.

Group 2 (operations)

The control group was a consecutive series of 22 patients treated from 1981 onwards. The 37 open surgical interventions included thrombectomy and grafting ($n=13$), short PTFE interposition ($n=14$) and short venous interposition ($n=10$).

The morphology of the lesions in groups 1 and 2 was similar in that they could have been dilated or operated upon. The length of the stenoses was shorter than 2 cm. During the study period one member of the surgical staff treated occlusions of haemodialysis fistulae by TA if possible while all of the other surgeons preferred open surgical methods.

There was no difference between the groups in terms of age and sex in that the mean age in group 1 was 52·2 years (range 33–74) and in group 2 it was 55·6 years (range 23–74). Group 1 comprised 15 men and 7 women while group 2 comprised 16 men and 6 women.

Patients were studied on the occasion of each dialysis, and at least once per week were assessed by clinical examination and invasive measurement of the fistula outflow pressure. In the case of pathological values, Doppler sonography and angiography were performed to determine the location and type of flow obstruction. The primary observer in the dialysis department and the radiologist concerned knew no details regarding previous treatment.

Patency rate in both groups was compared with a life table analysis (Kaplan–Meier plot, χ^2 test). Dead patients and those who did not attend for repeat examination (visitors, transplanted patients) were classified as lost to follow-up and excluded from all further evaluation.

Technique

The technique of percutaneous angioplasty was similar to that described by Gruentzig and Hopff[3]. We used thin double-lumen balloon catheters (F 7) with a 6–8 mm balloon diameter. The length of the balloon was as short as possible, and never longer than 2 cm, as we wished to avoid any trauma to the patent areas proximal and distal to the lesion. With these catheters we could keep the opening of the puncture as small as possible and enable moderate over-dilatation, especially at the site of the anastomotic sutures and very strong scars. Inflation time was 1 min and inflation pressure ranged up to 6 atm.

In cases of fistula stenosis without thrombotic occlusion we preferred the percutaneous route. In case of occlusion we prepared the vessels far from the anastomosis at a technically accessible site, carried out thrombectomy with a Fogarty catheter, and dilated the angiographically visible residual stenosis through a transverse vessel incision. Bleeding was controlled with a rubber tourniquet. Heparin solution was administered before passing through the stenosis with the catheter to avoid any occlusion of the thin fistula lumen. Surgical techniques were those of general vascular surgery.

Results

The cumulative patency rates in groups 1 and 2, respectively, were 94·5 and 78·1 per cent after 1 week, 72·3 and 64·1 per cent after 1 month, 31·3 and 19·3 per cent after 1 year, and 26·9 and

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Table 1 *Life table analysis of data from all dilated patients in group 1*

Follow-up period (months)	Number occluded	End of follow-up	Lost to follow-up	Open at the beginning of period	Cumulative patency rate	
					%	s.d.
0·00– 0·25	2	0	1	37	94·5	3·8
0·25– 0·50	3	0	0	34	86·2	5·7
0·50– 1·00	3	0	0	31	72·3	7·4
1·00– 3·00	3	0	0	28	61·2	8·1
3·00– 5·00	3	0	0	25	41·2	8·3
5·00–12·00	10	1	2	22	31·3	8·0
12·00–15·00	1	2	2	9	26·9	8·0

Table 2 *Life table analysis of data from all operated patients in group 1*

Follow-up period (months)	Number occluded	End of follow-up	Lost to follow-up	Open at the beginning of period	Cumulative patency rate	
					%	s.d.
0·00– 0·25	8	0	1	37	78·1	6·8
0·25– 0·50	3	0	0	28	69·7	7·6
0·50– 1·00	1	0	0	25	64·1	8·0
1·00– 3·00	5	0	0	24	44·4	8·3
3·00– 5·00	4	1	1	19	28·9	8·3
5·00–12·00	5	1	3	13	19·3	7·9
12·00–15·00	0	0	0	4	19·3	7·9

19·3 per cent after 15 months. The difference between the groups was statistically significant ($\chi^2 = 21{\cdot}9$, $P < 0{\cdot}001$) (*Tables 1* and *2*).

In group 1 there were two occlusions (5·4 per cent) and in group 2 there were six occlusions (16·2 per cent) within 24 h of treatment. This partially explains the significant difference in the patency rate of both groups. One venous perforation occurred as a complication of TA and two deep wound infections occurred after conventional operation.

Discussion

Transluminal angioplasty is of great value in the treatment of obstruction of the arteries of the pelvis, leg, kidney and heart[11]. This method has been used increasingly for the treatment of stenoses of haemodialysis fistula[6,12,13].

However, the literature gives no indication of the value of TA when compared directly with conventional methods of operation. The potential advantages of TA are obvious: short duration of procedure, little trauma to the vessel, less stress for the patient, fewer technical problems due to employment of a standardized technique, vascular access at a favourable site far from the stenosis or occlusion, and a lower complication rate. Furthermore, it is possible to dialyse immediately after treatment and interim solutions, such as the Scribner shunt or a central venous catheter, can be avoided. The disadvantages of TA are the use of contrast medium in patients with renal insufficiency and the need for technical equipment for radiology in the operating theatre. On the other hand, the large number of variations possible in open surgical methods may have led to a higher incidence of technical faults on the part of the surgeon. This contention is supported by our study in that early occlusion was more frequent in group 2 patients. In contrast to conventional operation, TA is always performed in conjunction with angiography which results in additional information becoming available for the surgeon.

In cases of fistula stenosis we prefer percutaneous TA as the infection rate is near to zero. If the fistula is occluded the length of the occlusion is usually 10 cm and more and the occlusion material consists of smooth thrombotic masses without organization to the vessel wall. These fresh thrombotic occlusions cannot be dilated as the danger of embolization to the pulmonary vessels is high. In these cases it seems better to thrombectomize the fistula using the Fogarty technique. Residual stenoses are then dilated intra-operatively.

The use of percutaneous transluminal angioplasty or intra-operative TA to treat fistula stenosis in no way restricts subsequent operations should they become necessary. Our study indicates that TA is now at least equivalent to, if not even better than, conventional operative techniques in the treatment of obstruction of haemodialysis fistulae.

References

1. Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction. *Circulation* 1964; **30**: 654.
2. Dotter CT, Roesch I, Judkins MP. Transluminal dilatation of arteriosclerotic stenosis. *Surg Gynecol Obstet* 1968; **127**: 794–804.
3. Gruentzig A, Hopff H. Die perkutane transluminale Rekanalisation chronischer Arterienverschluesse mit einem neuen Dilatationskatheter. *Dtsch Med Wschr* 1974; **99**: 2502.
4. Gruentzig A. Perkutane Rekanalisation chronischer Arterienverschluesse mit einer neuen Dilatationstechnik. 1st Edn. Baden-Baden, Köeln, New York: Witzstrock, 1977.
5. Rendl KH, Prenner K. 3 Jahre Erfahrungen mit der intraoperativen Angioplastie (ITA)—eine retrospektive Studie. *Langenb Arch Chir* 1983; **360**: 295–301.
6. Rendl KH, Prenner K. Die transluminale Angioplastie in der Behandlung von Komplikationen arteriovenöser Hämodialysefisteln. *Chirurg* 1983; **54**: 178–9.
7. Rendl KH, Prenner K. The redo-surgery of expanded polytetrafluoroethylene (PTFE) arteriovenous fistulas for hemodialysis. *Vasc Surg* 1984; **18**: 261–7.
8. Zeit RM, Constantin C. Failed hemodialysis shunts. One year experience with aggressive treatment. *Radiology* 1985; **154**: 353–6.
9. Rendl KH, Prenner K, Paulowitz HP. Die transluminale Dilatation bei der Behandlung von Komplikationen chronischer Hämodialysefisteln. *International Vascular Workshop* IV 1983 Zuers.
10. Valverde IP, Maillet R, Nussaume O. Sténoses des greffons d'hémodialyse. Traîtement par courte greffe. *La Presse Médicale* 1984; **13**: 32.
11. Novelline RA. Percutaneous transluminal angioplasty: newer applications. *Am J Rad* 1980; **135**: 983.
12. Heidler R, Zeitler E, Gessler U. Percutaneous transluminal dilatation of stenosis behind AV-fistulas in hemodialysis patients. In: *Percutaneous Vascular Recanalisation*. 1st Edn. Berlin, Heidelberg, New York: Springer, 1978: 142.
13. Reichelt HG. Perkutane transluminale Angioplastie bei insuffizientem Brescia-Cimino-Shunt. *Fortschr Roentgenstr* 1986; **2**: 183–9.

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Popliteal vein entrapment caused by the third head of the gastrocnemius muscle

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Three cases of the popliteal vein entrapment syndrome have been encountered during the past 3 years. The third head of the gastrocnemius muscle appeared to be the cause of this rare condition with the vessels in their normal position. Partial resection of the excess muscle was sufficient to relieve symptoms.

Keywords: Popliteal vein, gastrocnemius muscle, venous compression

Popliteal vascular entrapment syndrome is known to be caused by numerous muscle variations in the popliteal fossa. In most instances the symptoms are brought about by arterial occlusive changes and cases which showed venous symptoms have been rarely reported. Three cases which demonstrated venous symptoms have been encountered during the past 3 years and a characteristic finding was the presence of the well developed third head of the gastrocnemius muscle.

In this new entity, the third head of the gastrocnemius muscle arises from the medial head and the artery and vein are normally positioned. The anatomical relationship is illustrated in *Figure 1*.

Case reports

Case 1

A 23-year-old healthy woman, a bus-tour guide, was admitted, complaining of repeated episodes of bilateral calf swelling and pain after standing straight during her working hours for 1 year. Because of these symptoms, she gave up her job.

Physical examination revealed calf pain on squeezing and 2–3 cm increase in circumference after standing. Dorsiflexion of the ankle diminished peripheral arterial pulses. Bilateral femoral angiography revealed a normal popliteal artery and vein in neutral position. However, a slight stenosis of the artery was noted and almost complete occlusion of the vein in the passive dorsiflexion of the ankle. CT scanning showed a well developed medial head of the gastrocnemius muscle.

At operation, the right popliteal fossa was exposed through the posterior approach and an excess of muscle tissue was found over the popliteal neurovascular components (*Figure 2*). This excess muscle had attached at the mid-portion of the posterior surface of the femur and was easily detached from the medial head of the gastrocnemius muscle and resected, with relief of symptoms.

She recovered from her right calf symptoms. After 6 months the same operation was performed on the left side and 6 months later she resumed work as a bus-tour guide.

Case 2

A 16-year-old female student was admitted complaining of enlargement and of aching pain of the right calf after periods of prolonged standing over 1 year. Past history was not contributory.

On examination, tenderness was present in the right popliteal fossa. Pedal arterial pulses were absent on dorsiflexion of the ankle. Angiography appeared normal in neutral position, however on dorsiflexion of the ankle, the artery was completely occluded at the mid-portion of the popliteal artery with a slight lateral shifting (*Figure 3*). CT scanning revealed the same findings as in case 1. At surgery, an excess of the muscle was found in the popliteal fossa and was resected. Her postoperative course was uneventful. She still worries about a slight aching pain on the left side, but no surgery has been advised.

Case 3

A 14-year-old female student complained of swelling, aching pain, tiredness and a muscle cramp of the left calf for 6 months. On dorsiflexion of the ankle, the left popliteal artery showed a slight stenosis and the vein was completely occluded (*Figure 4*). Her past and family history was negative.

She underwent an operation in which the posterior exposure of the popliteal fossa was performed by a small horizontal skin incision. Excess muscle was found, as shown in pre-operative CT scanning, and was resected. She is now free of pain from the previously mentioned symptoms.

Discussion

Since anatomical abnormalities of this type were first described in 1879 by Stuart[1], numerous cases concerning the popliteal artery entrapment syndrome have been reported in medical literature[2–11]. These reports include the loop of the artery around the medial head of the gastrocnemius muscle, the passage of the artery through the medial head of the gastrocnemius muscle, the entrapment by fibrous bands or muscle slips, the venous entrapment alone or in combination with the artery and a normally positioned artery entrapped by aberrant muscle attachments. Because of the multiple causes of entrapment of the popliteal artery and vein, Rich[4] has

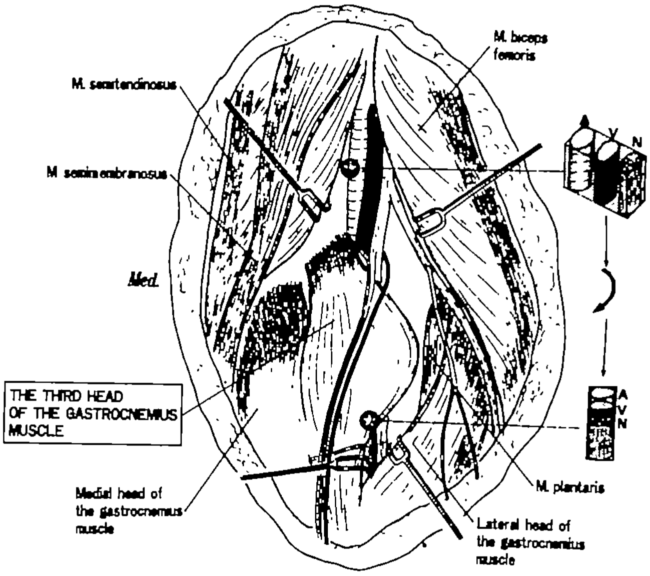
M. biceps femoris
M. semitendinosus
M semimembranosus
A
V
N
Med.
THE THIRD HEAD OF THE GASTROCNEMIUS MUSCLE
A
V
N
Medial head of the gastrocnemius muscle
M. plantaris
Lateral head of the gastrocnemius muscle

Figure 1 *Posterior aspect of the right popliteal fossa showing a well developed third head of the gastrocnemius muscle and its relationship with the surrounding neurovascular components*

This paper was presented on 26 September 1986 at the Ninth World Congress of Phlebology held in Kyoto, Japan

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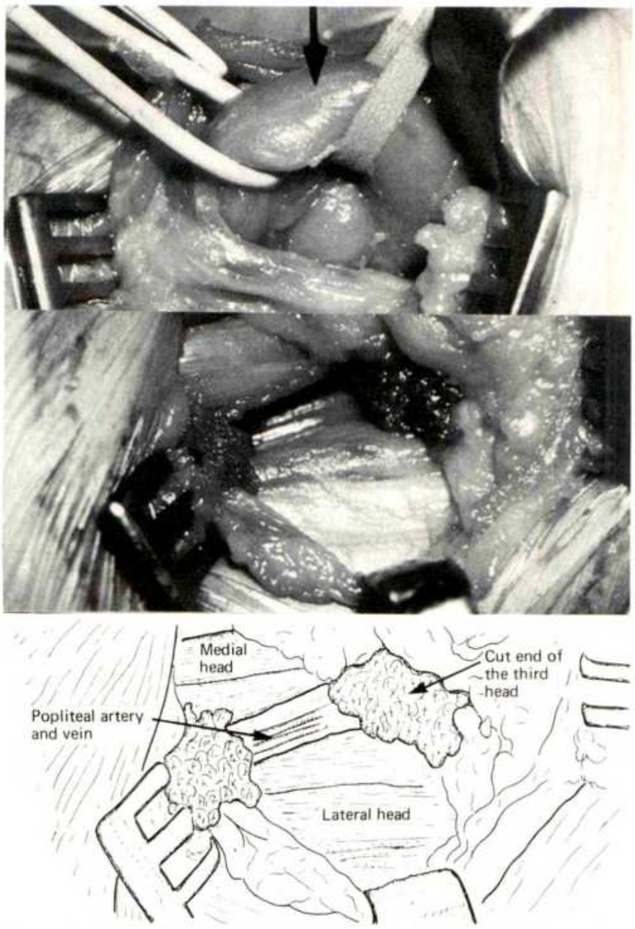

Figure 2 *Case 1, a 23-year-old woman showing her right popliteal fossa covered with an abnormal excess muscle (indicated by the arrow) between the medial and lateral gastrocnemius muscle (above) and free space after muscle resection (middle) with a line drawing to identify each structure (below). The right side is cephalad*

advocated the use of a new phrase, popliteal vascular entrapment syndrome, instead of popliteal artery entrapment syndrome[5].

Our experiences with the popliteal vascular entrapment syndrome, covering 14 arterial and 4 venous lesions during the past 10 years, are shown in *Table 1*. The venous lesions cases might seem to be quite large in number but this is a result of routinely checking, for 3 years, patients complaining of calf trouble by testing the dorsiflexion position of the ankle. This diagnostic manoeuvre already has been advocated by McDonald (1980)[6].

In this new entity, the third head of the gastrocnemius muscle arises from the medial head and the artery and vein are normally positioned (*Figure 1*). The characteristic signs and symptoms are: a history of leg swelling; aching pain; tiredness or muscle cramp of the calf after standing; and a tenderness of the popliteal fossa, which seems to be the result of chronic nerve compression. The next step to confirm diagnosis is to determine the distal arterial pulse diminution by passive dorsiflexion of the ankle.

Simple Doppler examination is valuable as an initial diagnostic evaluation. On placing the Doppler probe to the posterior tibial or dorsal pedis arteries, arterial sound will disappear on dorsiflexion of the ankle[7]. On the other hand, Doppler venous flow evaluation rarely gives accurate confirmation of the syndrome. Marked elevation of the venous pressure on dorsiflexion of the ankle may be a diagnostic indicator.

Patients may complain of calf expansion on dorsiflexion of the ankle or after standing for long periods with the knee straight. Another non-invasive diagnostic method is CT scanning of the popliteal region[3]. In our cases the excess muscle or well developed medial head-like muscle was observed and the artery and vein were located normally in the popliteal fossa (*Figure 5*). Angiography is most helpful in determining the cause of the vascular compression. Our cases showed lateral shift and complete or partial occlusive changes of the popliteal artery on dorsiflexion of the ankle. This change was thought to be insufficient to cause intermittent claudication. The venous phase of the angiogram is important and will demonstrate occlusive changes of the popliteal vein at the mid-portion. Secondary changes of the popliteal vein were not observed in our series. Patients with these findings might prove to have recent or old thrombus of the popliteal vein as demonstrated by phlebograms or at operation. Conversely, it is known that in a small number of patients with thoracic outlet syndrome, the phlebograms are normal in neutral position and exploration of the vein has not yielded evidence of a clot, though the clinical manifestations of

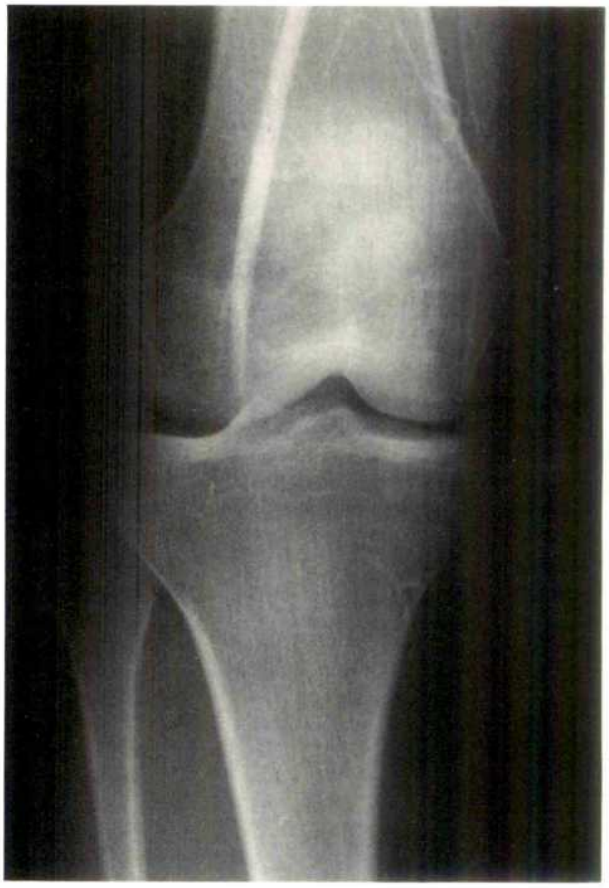

Figure 3 *Case 2, a 16-year-old girl showing complete popliteal arterial occlusion at the passive dorsiflexion of the right ankle*

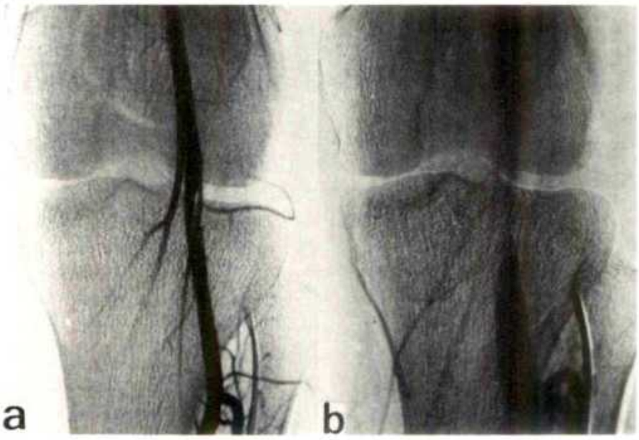

Figure 4 *Case 3, a 14-year-old girl.* **a**, *Slight stenosis of the artery and* **b**, *almost complete occlusion of the vein on dorsiflexion of the ankle*

Table 1 *Popliteal vascular entrapment syndrome (1975–86)*

Patient	Year	Age (years)	Sex	Side	Popliteal vein/artery at dorsiflexion of the ankle	Operation
Venous type					Popliteal vein	
1	1984	23	F	R	Occluded	RTG
	1985	23	F	L	Occluded	RTG
2	1984	16	F	R	Occluded	RTG
3	1986	14	F	L	Occluded	RTG
Arterial type					Popliteal artery	
1	1975	15	F	L	Thrombosed	TEA
	1976	16	F	R	Normal	SAR
2	1978	17	M	L	Thrombosed	SVG
	1978	17	M	R	Normal	DMR
3	1980	33	M	R	Thrombosed	SVG
4	1980	40	M	R	Thrombosed	SVG
5	1982	16	M	R	Thrombosed	SVG
	1982	16	M	L	Normal	SAR
6	1983	7	F	R	Thrombosed	SVG
7	1984	17	F	R	Normal	DB and RM
8	1984	23	M	R	Thrombosed	SVG
9	1985	24	M	R	Thrombosed	SVG
10	1985	73	F	R	Normal	*
	1985	73	F	L	Normal	*

RTG, resection of the third head of the gastrocnemius muscle; TEA, thrombo-endarterectomy; SAR, section of the artery and re-anastomosis; SVG, saphenous vein graft; DMR, division of the muscle and resuture; and DB and RM, division of the band and resection of the excess muscle; *, autopsy case

upper extremity deep venous obstruction are distinct[12]. Such a pathogenetic mechanism could apply to our cases.

Connell[8] has reported popliteal vein entrapment caused by an abnormal third head of the gastrocnemius muscle. In his patient, however, the third head originated from the medial head and was attached to the lateral side of the femur over the popliteal vein, so his case appears to differ from ours'. He also mentioned that the vein was simply compressed and did not show any thrombus formation of the vein. Rich[9] has reported popliteal artery and vein entrapment in which the vessels were looped over the medial head of the gastrocnemius muscle. This case also differs from ours'. We thus have concluded that our cases seem to vary from previously reported cases or classifications of the popliteal vascular entrapment syndrome[4,10,11].

The definition of the third head is a congenital growth of excess muscle, originating from the posterior and inferior surface of the femur, which joins the medial or lateral head of the gastrocnemius muscle. The literature concerning the third head[13,14] mentions that the joined muscle is more common with the medial head than with the lateral head. In Japanese people, the frequency rate of the third head is 5·5 per cent[14]. This seems to be high in comparison with other nationalities (2·9–3·4 per cent).

The surgical approach is to resect the excess muscle. Practically, the partial resection of the muscle is recommended to free space in the popliteal fossa. Postoperative use of a splint for 2–3 days is comfortable for patients. In our cases, the skin incision was horizontal and the length was 3–4 cm for cosmetic reasons.

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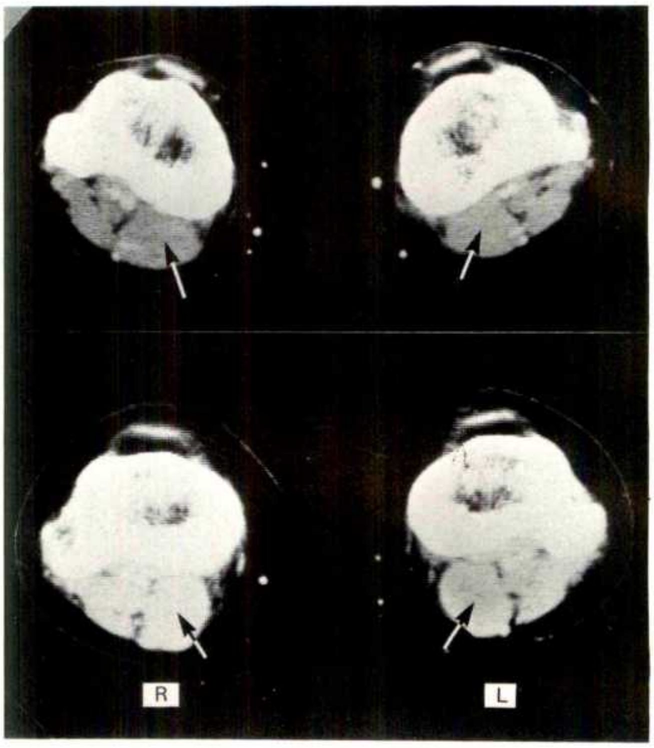

Figure 5 *CT scans showing quite large medial heads (arrowed) joined with the third head in case 1 (above) and case 2 (below). The artery and vein in the normal position*

References

1. Stuart TPA. Note on a variation in the course of the popliteal artery. *J Anat Physiol* 1879; **13**: 162.
2. Biemans RGM, van Bockel JH. Popliteal artery entrapment syndrome. *Surg Gynecol Obstet* 1977; **144**: 604–9.
3. Iwai T, Konno S, Soga K *et al.* Diagnostic and pathological considerations in the popliteal artery entrapment syndrome. *J Cardiovasc Surg* 1983; **24**: 243–9.
4. Rich NM, Collins GJ Jr, McDonald PT, Kozloff LK, Clagett GP, Collins JT. Popliteal vascular entrapment. Its increasing interest. *Arch Surg* 1979; **114**: 1377–84.
5. Love JW, Whelan TJ. Popliteal artery entrapment syndrome. *Am J Surg* 1965; **109**: 620–4.
6. McDonald PT, Easterbrook JA, Rich NM *et al.* Popliteal artery entrapment. *Am J Surg* 1980; **139**: 318–25.
7. Miles S, Roediger W, Cook P, Mieny CJ. Doppler ultrasound in the diagnosis of the popliteal artery entrapment syndrome. *Br J Surg* 1977; **64**: 883–4.
8. Connell J. Popliteal vein entrapment. *Br J Surg* 1978; **65**: 351.
9. Rich NM, Hughes CW. Popliteal artery and vein entrapment. *Am J Surg* 1967; **113**: 696–8.
10. Insua JA, Young JR, Humpheries AW. Popliteal artery entrapment syndrome. *Arch Surg* 1970; **101**: 771–5.
11. Delaney TA, Gonzalez LL. Occlusion of popliteal artery due to muscular entrapment. *Surgery* 1971; **69**: 97–101.
12. Adams JT, DeWeese JA, Hahoney EB, Rob CG. Intermittent subclavian vein obstruction without thrombosis. *Surgery* 1968; **63**: 147–64.
13. Frey H. Musculus gastrocnemius tertius. *Gegenbaurs Morph Jb*, 1919; **50**: 517–30.
14. Tochihara J, Onozawa T. M. gastrocnemius tertius in Japanesa. *Jpn J Anat* 1932; **5**: 589–600.

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Prognostic significance of oestrogen and progestogen receptor activities in breast cancer

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The prognostic significance of the tumour activities of 2 steroid receptors, those for oestrogen (ER) and for progestogen (PgR), has been studied in 372 patients with breast cancer, in whom follow-up was available for 2–6 years (median 41 months). Of 252 patients with operable disease, 75·8 per cent had ER-positive tumours and 46·4 per cent had PgR-positive tumours, though a small additional fraction (6·3 per cent) had an equivocal PgR assay result. For the 236 patients with unequivocal receptor status, the relationships between disease-free interval or overall survival and receptor activity and other factors were evaluated by univariate and multivariate analyses. The latter revealed that only tumour size, node status, menstrual status and ER status related significantly to both disease-free interval and survival, though adjuvant therapy also related to disease-free interval, and tumour grade related to survival. It is concluded that measurements of PgR activity do not add to the prognostic significance of ER status.

Keywords: Oestrogen receptor, progestogen receptor, prognosis breast cancer

In 1975 McGuire, Pearson and Segaloff[1] noted that patients with oestrogen receptors (ER) in their tumours have a better prognosis than patients whose tumours are devoid of such receptors. Since that time, many other groups[2–21] have examined the value of the oestrogen receptor as a prognostic factor and, although most have confirmed the relationship between the presence of receptors and prolonged overall survival, the relationship between oestrogen receptor status and disease-free interval has proved controversial. In 1975, Horwitz and her colleagues[22] drew attention to the potential value of a second steroid receptor, the progestogen receptor (PgR) and subsequent studies[3,12,14,17,19] have suggested that the progestogen receptor may be a better prognostic indicator than the oestrogen receptor.

In the present study, we report our own findings on 372 cases of primary breast cancer in whom both oestrogen receptor and progestogen receptor activities were assayed at the time of presentation, and in whom follow-up has been continued for between 2 and 6 years.

Patients and methods

Patients

In 372 patients, sufficient tumour was obtained for both ER and PgR assays. Of these, 16 cases were excluded for various reasons (e.g. notes lost) and 104 were classified as having advanced disease, either locally inoperable or metastatic (*Figure 1*). Of the remaining 252 assays, performed on operable primary carcinomas (T_1, T_2 and some $T_3 N_{0-1b}$) at the time of presentation, 16 showed PgR assay results which could not be classified as either clearly positive or negative; these have been termed 'equivocal' and excluded from the subsequent major analysis, leaving a data base of 236 cases.

For each patient, the date of birth, date of assay, clinical size of lesion, menstrual status, initial local therapy, type of adjuvant therapy (if any), date and site of first recurrence and date of death or last review were recorded. For the classification of menstrual status, patients were divided into premenopausal (<12 months after the last menstrual period) or postmenopausal (>12 months after the last menstrual period, hysterectomized–ovariectomized or hysterectomized and >50 years of age).

Histology

Before steroid receptor assay, a thin slice was cut from the face of each tumour, fixed in formol–saline and embedded in paraffin wax. Histological sections were cut and stained with haematoxylin and eosin. These sections were retrospectively examined under the microscope to confirm the presence of tumour, and scored for tumour grade (scale 1, 2 or 3) as described by Bloom and Richardson[23], for elastosis (scale, −, + or ++) as described by Shivas and Douglas[24], and for tumour cellularity (proportion of the specimen occupied by malignant epithelial cells on a scale from 1 to 16) as we have described previously[25]. Tumours were also classified[26] as 'special type' or 'no special type'.

From the main histopathology report, tumours were designated as node-negative or node-positive; all the other histological assessments were performed by one of us (J.M.J.D.) in ignorance of the receptor assay results.

Determination of steroid receptor activities

After removal of a section from the face of each tumour sample for histological examination, the remainder of the tissue was used for steroid receptor assays. For ER activity, the tissue was homogenized in Tris buffer (10 mM Tris, 0·25 M sucrose, 1 mM ethylene diamine tetracetate, pH 8·0 at 22°C plus 1 per cent volume/volume monothioglycerol and 10 per cent volume/volume glycerol) and centrifuged at low speed to yield a supernatant cytosol which was used in a saturation analysis as previously described[25]. Progestogen receptors were assayed either on the same cytosol, using Organon-2058 (Amersham International PLC) as previously described[25], or by homogenization of an adjacent portion of tumour in Tris buffer (10 mM Tris, 0·25 M sucrose, 1·5 mM EDTA, and 0·5 mM dithiothreitol) and centrifuged at high speed to yield a supernatant cytosol which was assayed using R5020 as previously described[27]. For each type of receptor, the dissociation constant of binding and the concentration of receptor sites were determined by Scatchard[28] analysis and the total soluble protein content of each cytosol was determined by the method of Bradford[29]. Receptor concentrations were expressed as femtomoles of binding sites per milligram of soluble protein. Tumours were designated as ER-positive when they contained >5 fmol of binding sites/mg of protein, and PgR-positive when they contained either >10 fmol of sites/mg protein using Organon-2058 or >15 fmol of sites/mg protein using R5020, these figures being selected according to the sensitivity of the assays. In some cytosols (16 primary, 12 advanced, *Figure 1*), although a small number of counts of radioligand were displaced by the

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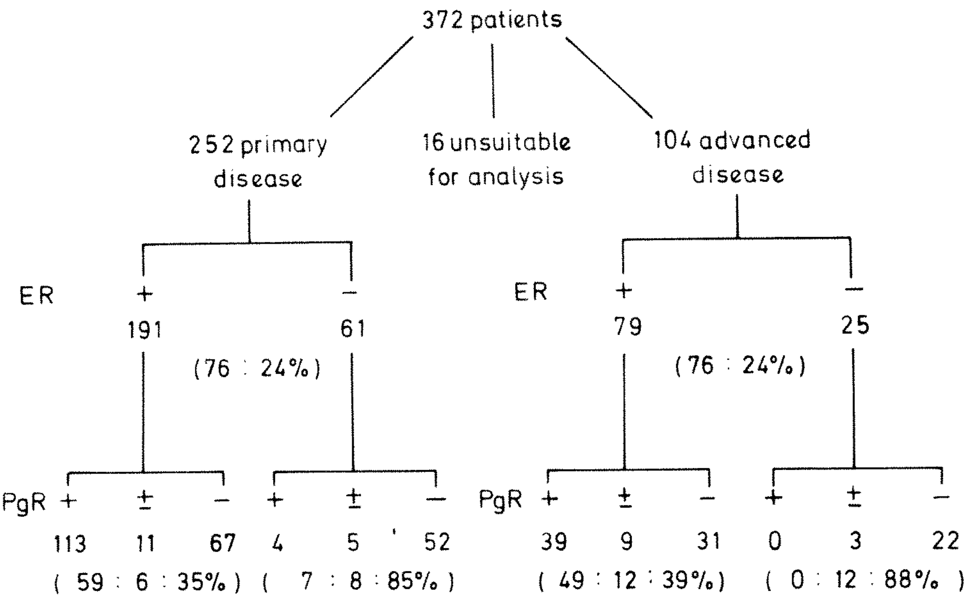

Figure 1 *Summary of patients studied. The patients in whom progestogen receptor status was equivocal (±) were excluded from all the subsequent analyses. By χ^2 test, PgR were present significantly more frequently in ER-positive tumours than in ER-negative tumours* (P<0·001 *for either primary disease or advanced disease)*

addition of non-radioactive competitor, it was not possible to draw any Scatchard plot and assess the dissociation constant of binding; equally, it was not possible to designate these tumours as PgR-negative and the tissues were accordingly classed as PgR equivocal and omitted from the subsequent major analysis.

Statistics

Preliminary analysis of the inter-relationship between ER and PgR and of the influence of other factors on receptor status was made by χ^2 tests.

Curves for both survival time and disease-free interval were then calculated by the Kaplan–Meier method, using BMDP[30]. All deaths with cancer were considered to be related to the effects of the primary disease, and deaths from other causes (three cases) were treated as censored data.

A univariate analysis of the importance of each prognostic factor was performed using the log rank test to compare the survival/disease-free interval distributions at the various levels or categories for the prognostic factor concerned.

Finally, a multivariate analysis by Cox's proportional hazards regression model was used to compare the prognostic value of various combinations of factors and, in particular, to determine whether or not progestogen receptor status had an additional value once the other factors had been considered. In this analysis, prognostic factors are added in a step-wise manner; at each step, the next factor to be included was the one which exerted the greatest effect on the prognostic value of the factors already selected, until no further significant improvement could be made.

Two-tailed tests were used in all analyses.

Results

Incidence of oestrogen and progestogen receptor activities

A breakdown of the total group of 372 patients is summarized in *Figure 1*. Of the 252 patients, with operable disease, 75·8 per cent had ER-positive tumours, 46·4 per cent were classified as clearly PgR-positive and 47·2 per cent as PgR-negative. The breakdown from patients presenting with advanced disease was very similar.

Relationship of oestrogen receptors to progestogen receptors

Tumours were more likely to be PgR-positive when ER were present than when ER were absent (*Figure 1*, $P<0·001$ by χ^2 test). Furthermore, the incidence of PgR-positives rose significantly ($P<0·05$, test of trend) as the tumour ER concentration increased (*Figure 2*).

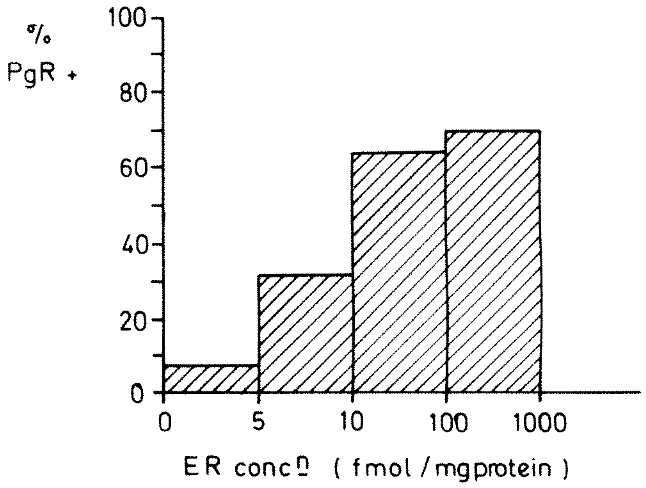

Figure 2 *Relationship between PgR status and ER concentration in 236 primary breast cancers*

Relationship of nodal status, menstrual status, tumour grade, initial treatment and adjuvant therapy to receptor status

A more detailed breakdown of the patients with operable disease is shown in *Table 1*. Neither nodal status nor tumour size was related to the incidence of the steroid receptor activities. However, whilst menstrual status had no effect on the incidence of PgR, ER activity was found significantly more frequently in postmenopausal women than premenopausal women, and both ER and PgR activities were significantly more common in the more differentiated (grades I and II) than in the anaplastic tumours (grade III).

When the patients were broken down according to their initial treatment or type of adjuvant therapy, ER status and PgR status were found to be similarly distributed in the various treatment groups.

Relationship of potential prognostic factors to disease-free interval and survival

Univariate analysis. Each of the potential prognostic factors, ER status, PgR status, menstrual status, node status, tumour size, tumour grade, histological type, cellularity and elastosis, when examined separately by univariate analysis, was

Table 1 *Relationship between receptor status and other factors in 236 patients with operable primary breast cancer*

Factor	% ER+	P value	% PgR+	P value
Node status				
N−	79	n.s.	51	n.s.
N+	74		48	
Menstrual status				
Pre-	67	0·02	55	n.s.
Post-	81		47	
Tumour grade				
I	98		66	
II	86	0·01	60	0·01
III	48		24	
Tumour size				
< 2 cm	78		53	
2–5 cm	78	n.s.	50	n.s.
5 cm	62		38	
Initial treatment				
Mx + sample	81		35	
Mx + sample + XRT	75	n.s.	55	n.s.
Mx + clearance	72		27	
Adjuvant therapy				
Tamoxifen	76		48	
Other	77	n.s.	65	n.s.
None	76		47	
All patients	76		50	

ER, oestrogen receptor; PgR, progestogen receptor; Mx, mastectomy; sample, node sampling; clearance, clearance of the axillary nodes; XRT, radiotherapy. Percentages refer to the proportion of R-positive: R-negative tumours with each horizontal group. *P* values refer to the significance of the χ^2 test of independence of receptor status from each factor

Table 2 *Relationship of prognostic factors to disease free interval and survival by univariate analysis*

Prognostic factor	*P* value	
	DFI	Survival
Tumour grade	< 0·001	< 0·001
ER status	0·001	0·001
Node status	0·002	< 0·001
PgR status	0·011	0·008
Menstrual status	0·012	0·007
Tumour size	0·014	0·001
Cellularity	0·030	0·019
Histological type	0·057	0·026
Elastosis	0·080	0·013

Probability of survival from log rank test. DFI, disease free interval; ER, oestrogen receptor; PgR, progestogen receptor

significantly related to survival, i.e. survival was longer in patients with ER-positive or PgR-positive tumours, premenopausal status, negative nodes, smaller tumours, more differentiated tumours, less cellular tumours and more elastosis (*Table 2*). A similar relationship existed between these factors and disease-free interval with the exception of elastosis: the influence of the latter upon disease-free interval did not attain significance ($P = 0{\cdot}08$).

As a single prognostic factor, ER status was of greater value than PgR. The relationships of these two factors to disease-free interval and survival are illustrated in *Figures 3* and *4*.

Multivariate analysis. The relationship of the potential prognostic factors to survival and disease-free interval was re-examined using multivariate analysis by Cox's model. The directions of effect of the factors included in this model (*Table 3*) were in accord with those found in the univariate analysis described above. Of the various factors examined, however, only tumour size, node status, menstrual status and oestrogen receptor status were significantly related to both disease-free interval and survival. In addition, systemic adjuvant therapy was significantly related to disease-free interval and tumour grade related to survival. Other factors and, in particular, the progestogen receptor status, were found not to add to the prognostic power of the factors listed above (*Table 3*).

Discussion

The present results confirm, in a series of operable breast cancers that, on their own, each of many factors can have prognostic significance relating to both disease-free interval and survival. These factors include tumour grade, ER status, PgR status, size, cellularity and histological type, node status and menstrual status; the degree of elastosis in the tumour, in addition, was related only to survival. Such results are in agreement with earlier studies by ourselves and others (for example[1–6,12,18,19,22,31,32]). However, many of these prognostic factors are interrelated (for example PgR and ER). After a multi-variate analysis only tumour size, node status, ER status and menstrual status exerted significant effects on both disease-free interval and survival. Disease-free interval was additionally influenced by adjuvant therapy and survival by tumour grade.

Our findings differ significantly from those reported by some groups in the USA[3], France[12,14,17] and Italy[19] but agree with those of several other centres[7,15,33] and in particular with those of Sutton and his colleagues[21]. The reasons for these differences are not clear.

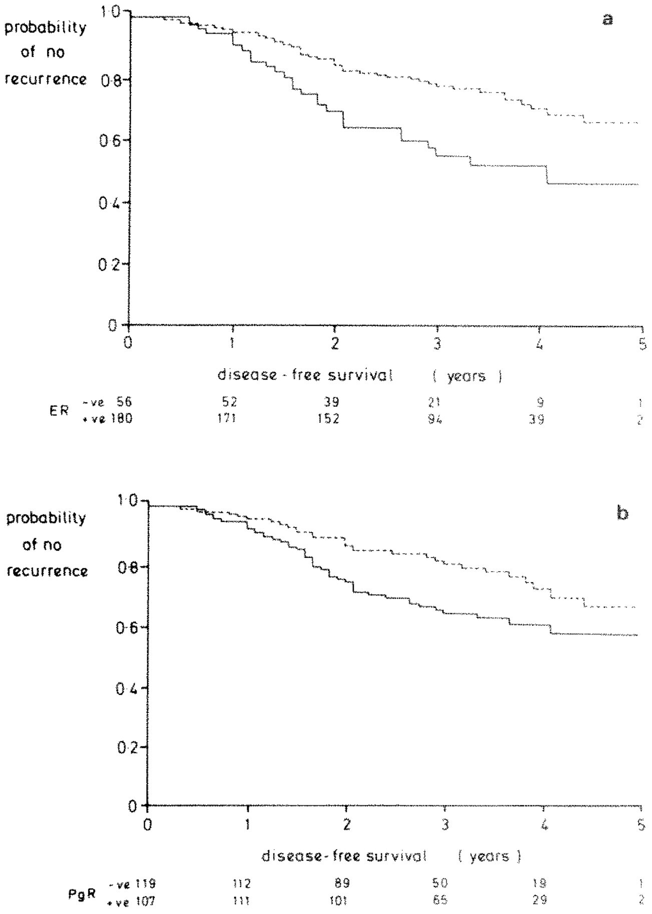

Figure 3 *Effect of* **(a)** *ER status and* **(b)** *PgR status on disease-free interval in 236 patients with primary breast cancer.* ——, *ER- and PgR-negative;* - - -, *ER- and PgR-positive.* P = *0·001 for ER-positive/negative comparison and* P = *0·001 for PgR-positive/negative comparison*

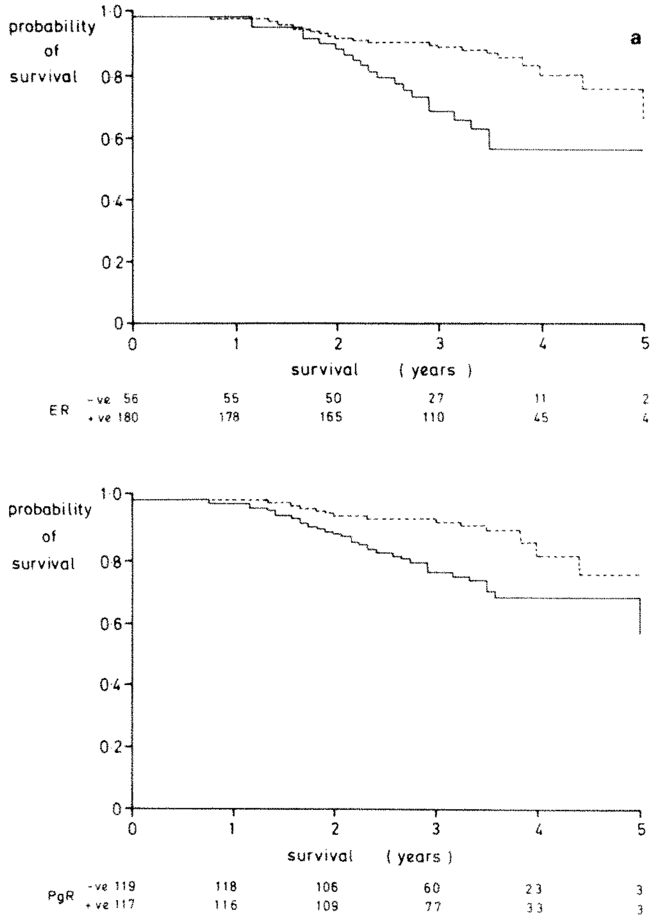

Figure 4 *Effect of* (**a**) *ER status and* (**b**) *PgR status on survival in 236 patients with primary breast cancer.* ——, *ER- and PgR-negative;* - - -, *ER- and PgR-positive.* P=*0·001 for ER-positive/negative comparison and* P=*0·008 for PgR-positive/negative comparison*

Early studies suggested that PgR activity is a better marker of endocrine responsiveness than ER[21,34] and our own studies have shown that differences in PgR were greater than those in ER in experimental tumours of known hormonal sensitivity[35]. However, fundamental studies have demonstrated that stimulation of PgR synthesis is not necessarily a marker of a functional ER protein[36] and preliminary analysis of the 104 advanced cases (not included here) suggests that PgR-positive tumours are evenly divided amongst the responders and non-responders to endocrine therapy in our patients.

The assay of PgR activity is technically more demanding than that for ER, but the incidence of PgR-positive tumours reported here is comparable to those found in other series and methodological defects seem unlikely to account for our findings. One possible reason for the conflicting findings in different centres, however, may be the 'lability' of PgR status with time, since Raemaekers *et al.*[37] have shown that, at least in advanced disease, PgR measurements are predictive only for treatments given close to the time of assay. Whatever the cause of the uncertainty about the significance of PgR measurements, the question is of importance since it may influence management costs. In the UK the case for funding assays for PgR, in addition to those for ER, has generally been considered unproven.

In summary, our study of 236 cases of operable primary breast cancer has confirmed the prognostic significance of established factors such as T and N staging and ER status. No additional benefit was detected in measuring PgR activity. It should be noted, however, that the median follow-up in this series is relatively short and some studies show that the factors with prognostic significance over a longer time (i.e. 4–7 years) may well be different from those important in the short-term[8,12,13,20].

Table 3 *Relationship of prognostic factors to disease-free interval and survival by multivariate analysis*

Prognostic factor	*P* value	
	DFI	Survival
Factors included in the model		
Tumour size	<0·001	<0·001
ER status	<0·001	0·042
Menstrual status	0·005	0·006
Node status	0·017	<0·001
Adjuvant therapy	0·043	—
Tumour grade	—	0·006
Factors rejected from the model		
Cellularity	0·057	0·570
Tumour grade	0·066	—
Elastosis	0·077	0·133
Histological type	0·096	0·305
Initial therapy	0·203	0·877
Adjuvant therapy	—	0·406
PgR status	0·405	0·501

P values refer to the level of the likelihood ratio test for removal from or entry into the model of each factor. DFI, disease free interval; ER, oestrogen receptor; PgR, progestogen receptor

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References

1. McGuire WL, Pearson OH, Segaloff A. Predicting hormone responsiveness in human breast cancer. In: McGuire WL, Carbone PP, Vollmer EP, eds. *Estrogen Receptors in Human Breast Cancer*. New York: Raven Press, 1975: 37–56.
2. Walt AJ, Singhakowinta A, Brooks SC *et al.* The surgical implications of estrophile protein estimations in carcinoma of the breast. *Surgery* 1976; **80**: 506–12.
3. Clark GH, McGuire WL. Prognostic factors in primary breast cancer. *Breast Cancer Res Treat* 1983; **3** (Suppl 1): 69–72.
4. Nicholson RI, Campbell FC, Blamey RW, Elston CW, George D, Griffiths K. Steroid receptors in early breast cancer. *J Steroid Biochem* 1981; **15**: 193–9.
5. Croton R, Cooke T, Holt S, George WD, Nicholson R, Griffiths K. Oestrogen receptors and survival in early breast cancer. *Br Med J* 1981; **283**: 1289–91.
6. Mason BH, Holdaway IM, Mullins PR, Yee LH. Progesterone and estrogen receptors as prognostic variables in breast cancer. *Cancer Res* 1983; **43**: 2985–90.
7. Stewart JF, Rubens RD, Millis RR, King RJB, Hayward JL. Steroid receptors and prognosis in operable (Stage I and II) Breast Cancer. *Eur J Cancer Clin Oncol* 1983; **19**: 1381–7.
8. Howell A, Barnes DM, Harland RNL *et al.* Steroid hormone receptors and survival after first relapse in breast cancer. *Lancet* 1984; **i**: 588–91.
9. McLelland RA, Powles TJ, Coombes RC. Oestrogen receptors and prognosis in disseminated breast cancer. British Association Cancer Research, Manchester, 1984; **7**: 18 (Abstract).
10. Godolphin W, Elwood JM, Spinelli JJ. Estrogen receptor quantitation and staging as complementary prognostic factors in breast cancer: a study of 583 patients. *Int J Cancer* 1981; **28**: 677–83.

11. Humeniuk V, Hawkins RA, Prescott RJ, Roberts MM, Stewart HJ, Forrest APM. Oestrogen receptors and primary breast cancer. *Aust NZ J Surg* 1982; **52**: 408–14.
12. Saez S, Cheix F, Asselain B. Prognostic value of estrogen and progesterone receptors in primary breast cancer. *Breast Cancer Res Treat* 1983; **3**: 345–53.
13. Hahnel R, Woodings T, Vivian AB. Prognostic value of estrogen receptors in primary breast cancer. *Cancer* 1979; **44**: 671–5.
14. Pichon MF, Pallud C, Brunet M, Milgrom E. Relationship of presence of progesterone receptors to prognosis in early breast cancers. *Cancer Res* 1980; **40**: 3357–60.
15. Kinne DW, Ashikari R, Butler A, Menendez-Botet CJ, Rosen PP, Schwartz M. Estrogen receptor protein in breast cancer as a predictor of recurrence. *Cancer* 1981; **47**: 2364–7.
16. Hilf R, Feldstein ML, Gibson SL, Savlov ED. The relative importance of estrogen receptor analysis as a prognostic factor for recurrence or response to chemotherapy in women with breast cancer. *Cancer* 1980; **45**: 1993–2000.
17. Magdelenat H, Pouillart P, Jouve M *et al.* Progesterone receptor as a more reliable prognostic parameter than estrogen receptors in patients with advanced breast cancer (letter). *Breast Cancer Res Treat* 1982; **2**: 195.
18. Samaan NA, Buzdar AV, Aldinger KA *et al.* Estrogen receptor: a prognostic factor in breast cancer. *Cancer* 1981; **47**: 554–60.
19. Bertuzzi A, Vezzoni P, Ronchi E. Prognostic importance of progesterone receptors (PR) alone or in combination with estrogen receptors (ER) in node-negative (N –) breast carcinoma (abstract). *Proc Am Assoc Clin Oncol* 1981; **22**: 447.
20. Adami HO, Graffman S, Lindgren A, Sallstrom J. Prognostic implications of estrogen receptor content in breast cancer. *Breast Cancer Res Treat* 1985; **5**: 293–300.
21. Sutton R, Campbell M, Cooke T, Nicholson RI, Griffiths K, Taylor I. Predictive power of progesterone status in early breast carcinoma. *Br J Surg* 1987; **74**: 223–6.
22. Horwitz KB, McGuire WL, Pearson OH, Segaloff A. Predicting response to endocrine therapy in human breast cancer: a hypothesis. *Science* 1975; **189**: 726–7.
23. Bloom HJG, Richardson WW. Histological grading and prognosis in breast cancer: a study of 1409 cases of which 359 have been followed for 15 years. *Br J Cancer* 1959; **11**: 359–77.
24. Shivas AA, Douglas JG. The prognostic significance of elastosis in breast cancer. *J R Coll Surg Edinb* 1972; **17**: 315.
25. Hawkins RA, Black R, Steele RJC, Dixon JMJ, Forrest APM. Oestrogen receptor concentration in primary breast cancer and axillary node metastases. *Breast Cancer Res Treat* 1981; **1**: 245–51.
26. Dixon JM, Page DL, Anderson TJ *et al.* Long-term survivors after breast cancer. *Br J Surg* 1985; **72**: 445–8.
27. Miller WR, Telford J, Hawkins RA. Binding of [^{3}H]-methyltrienolone (R1881) by human breast cancers. *Eur J Cancer Clin Oncol* 1983; **19**: 1473–8.
28. Scatchard G. The attraction of proteins for small molecules and ions. *Ann NY Acad Sci* 1949; **51**: 660–72.
29. Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem* 1976; **72**: 248–54.
30. Dixon WJ, ed. *BMDP Statistical Software.* Berkeley: University of California Press, 1981.
31. Langlands AO, Kerr GR. Prognosis in breast cancer: the relevance of clinical staging. *Clin Radiol* 1978; **29**: 599–606.
32. Black R, Prescott R, Bers K, Hawkins RA, Stewart HJ, Forrest APM. Tumour cellularity, oestrogen receptors and prognosis in breast cancer. *Clin Oncol* 1983; **9**: 311–18.
33. Raemaekers JM, Beex LV, Koenders AJ *et al.* Concordance and discordance of oestrogen receptor and progesterone receptor contents in sequential biopsies of patients with advanced breast cancer in relation to survival. *Eur J Cancer Clin Oncol* 1984; **20**: 1011–18.
34. Knight WA, Osborne CK, Yochmowitz MG, McGuire WL. Steroid hormone receptors in the management of human breast cancer. *Ann Clin Res* 1980; **12**: 202–7.
35. Hawkins RA, Tesdale A, Freedman B, Telford J, Miller WR. Progestogen and oestrogen receptor activity in ovary-dependent and ovary-independent tumours of the rat. *Eur J Cancer* 1981; **17**: 585–7.
36. Yu WCY, Leung BS, Gao YL. Effects of 17-estradiol on progesterone receptors and the uptake of thymidine in human breast cancer cell line CAMA-1. *Cancer Res* 1981; **41**: 5004–9.
37. Raemaekers J, Beex L, Koenders A *et al.* Quantitative progesterone receptor activity (PgR) and response to first endocrine therapy in advance of breast cancer. Progesterone receptor activity (PgR) and response to first endocrine therapy in advanced breast cancer: significance of timing of receptor analysis. *Eur J Cancer Clin Oncol* 1986; **22**: 731 (Abstracts 1–8 and 1–9).

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Reduction of the surgical excision rate in benign breast disease using fine needle aspiration cytology with immediate reporting

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Patients attending a breast clinic in two different periods were studied. In the first period fine needle aspiration cytology (FNAC) was not available and in the second it was used on all discrete solid breast lumps and reported immediately in the clinic. With the use of FNAC the overall surgical excision rate for discrete solid lumps was reduced from 83 per cent to 41 per cent and the excision rate in patients with benign disease was reduced from 74 per cent to 23 per cent ($P < 0{\cdot}001$). All patients with breast cancer in the second period had malignant cytology and no patient with benign or acellular cytology has been shown, after a minimum follow-up period of 18 months, to have breast cancer. Using FNAC with immediate reporting, the number of operations performed in patients with benign breast disease can be safely reduced.

Keywords: Fine needle aspiration cytology, diagnosis of breast disease, breast biopsy

Fine needle aspiration cytology (FNAC) is widely used to diagnose malignant breast lesions[1-5]. Its use in the diagnosis of benign lesions with the avoidance of surgical excision has, however, not been investigated.

This study set out to determine whether FNAC reported immediately in the breast clinic could reduce the number of operations performed in patients with benign disease, while at the same time detecting all patients with breast cancer.

Patients and methods

Two groups of patients were studied:

1. One hundred and fifty-four patients presenting consecutively to the breast clinic in the 3-month period immediately before FNAC became available in the clinic;
2. Two hundred and six patients presenting consecutively to the breast clinic in the 3-month period immediately after FNAC had become established in the clinic. This followed an initial trial period of FNAC[6]. During this second period FNAC was performed on all solid breast lumps and reported immediately in the breast clinic. The increase in numbers of patients during the second 3-month period was due to an increased number of referrals.

The clinic protocol during both periods of study included clinical examination by a senior member of staff. All discrete breast lumps were assessed clinically as malignant, suspicious of malignancy or benign. Patients over the age of 35 years with a discrete mass underwent mammography. This was also reported as malignant, suspicious, benign or normal. In the second 3-month period patients with discrete lumps had mammography performed and reported on the same day as their clinic visit.

Throughout both periods all discrete masses were needled and, if cystic, were aspirated. In the first 3 months if a lesion was solid then FNAC was not undertaken, whereas in the second 3-month period all patients over the age of 16 years with a discrete mass and some with nodularity had FNAC performed using a standard technique[4]. Smears from solid lesions were prepared immediately and reported in the clinic after staining with the Diff Quick technique[7] by a single cytologist (V.C.) Two smears were processed and reported as malignant, suspicious of malignancy, benign or acellular. The next day the remainder of the material was prepared and stained by both May–Grünwald Giemsa and Papanicolaou techniques. A supplementary report was issued if the assessment of these smears differed from the original report.

Indications for surgical excision

In the first 3 months it was policy to excise all discrete solid breast lumps. If mammography was performed, patients were reviewed 3 weeks later. If (using calipers) the lump had decreased in size, then the patient was reviewed at 6 weeks, 3 months and 6 months or until the lump could no longer be palpated.

In the second 3-month period excision was performed in a patient with a discrete breast lump only when: (1) the patient wished the lump to be removed; (2) results of cytological examination were suspicious or malignant; (3) a lesion was clinically malignant but results of cytological examination were benign or acellular, or (4) a mass gave rise to clinical suspicion and results of cytological examination were acellular. All remaining patients with discrete lumps with benign or acellular cytology were reviewed in the breast clinic on at least two further occasions over an 18-month period.

Comparison of excision rates during the two study periods was performed using the χ^2 test.

Results

First period—no FNAC

In the first period 47 (30·5 per cent) patients seen in the clinic had a discrete solid mass on examination, of which 39 were surgically excised, an excision rate in this group of 83 per cent (*Table 1*). All eight patients who did not have a biopsy had reduction in size of the lump on clinical review following mammography. None of these eight patients had subsequently undergone biopsy or has been shown to have breast cancer. In the 39 solid masses excised, 16 carcinomas were identified. Therefore, of the 47 patients presenting with discrete lumps, 31 were finally considered to be benign and 23 had their lump

Table 1 *Summary of clinical findings of patients during two study periods*

	Numbers of patients	
	First period	Second period
Total	154	206
Cysts	12 (7·8%)	16 (7·8%)
No discrete mass	95 (61·7%)	122 (59·2%)
Discrete solid mass	47 (30·5%)	68 (33%)
Masses not excised	8	40
Masses excised	39	28
Benign on biopsy	23	12
Malignant on biopsy	16	16

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Table 2 *Indications for biopsy in second period when cytological examination was available in the clinic*

Indication*	Number of patients
Mass + M cytology	16
Mass + S cytology	2
Mass clinically M + B cytology	2
Patient demand	8
Total	28

* M, malignant; S, suspicious; B, benign

excised, a surgical excision rate in the benign group of 74 per cent. Of these 23 benign biopsies, 9 were fibroadenomas and 14 were so-called 'fibrocystic disease'.

Second period–with FNAC

In the second period 68 (33 per cent) patients presenting to the clinic had a discrete solid mass on examination (*Table 1*). During this time 28 of these were surgically excised, an excision rate of 41 per cent. The indications for excision are shown in *Table 2*.

Sixteen patients with breast carcinoma were identified in the group of twenty-eight who underwent surgical excision: therefore, twelve of the twenty-eight patients who had an open biopsy had benign disease. All 16 patients with breast carcinomas had malignant cytology, these being the only 16 lesions reported as malignant on cytological examination. Thus, in this period the sensitivity of FNAC for malignancy was 100 per cent. One of these lesions was considered to be benign on clinical examination and two were reported to be benign on mammography.

Twelve of the fifty-two patients (23 per cent) whose lesions were eventually considered to be benign had their lump excised: this was a significant reduction from the rate of solid benign masses excised (74 per cent *versus* 23 per cent) in the first 3-month period ($P<0.001$, χ^2 test). Eight were removed because of patient demand. In these, cytological examinations were performed on four and gave benign results in all four. Two patients had a biopsy because of suspicious cytology. The smears from one of these patients were originally considered in the clinic to be benign, but were subsequently reported the next day as suspicious. This represents the only patient in whom further assessment of all the aspirated material altered the cytological diagnosis given in the clinic. Both the biopsies performed for suspicious cytology demonstrated benign disease with hyperplasia. Two other patients with clinically malignant lumps and benign cytology were also biopsied. Histology confirmed the benign nature of both lesions. Of the 12 benign lesions excised, 7 were fibroadenomas, 4 were reported as showing 'fibrocystic disease' and 1 showed periductal mastitis.

Forty of the fifty-two patients with discrete solid benign lesions did not undergo surgical excision (*Table 1*) and FNAC was performed on 34. The remaining six patients did not have cytological examinations because three were young (<16 years) and considered to be outside the age group at risk of breast cancer; two patients who both presented with breast pain had lumps, which had been previously investigated in the clinic by mammography and shown to be calcified fibroadenomas and one patient had multiple lumps, which on review 3 weeks later had almost totally disappeared. Cytology was reported as benign in 22 of the 34 patients who had FNAC and acellular in 12. None of these 40 patients has been shown to have breast cancer during a follow-up period ranging from 18 to 21 months. If one includes acellular smears as confirming benign disease, then FNAC had a specificity of 95 per cent and an accuracy of 96 per cent in discrete solid lumps during this second study period.

It should be emphasized that all the above lesions, during both periods, were considered to be discrete lumps by the senior clinician examining the patient. Six patients with nodular areas in the upper outer quadrant of the breast had an open biopsy in the first 3 months studied. In the second 3 months FNAC was performed on 12 patients with non-discrete lumps: 7 were reported as benign and 5 as acellular. None of these patients has come to open biopsy or has subsequently been shown to have breast cancer.

Discussion

The combination of clinical examination and mammography does not allow identification of all patients with malignant breast lesions[8,9]. Because of this, it is practice in Britain to excise all discrete solid breast masses. This practice results in large numbers of patients undergoing a biopsy for benign conditions, a procedure which is not without morbidity[10–11], J. M. Dixon, A. P. M. Forrest and U. Chetty, unpublished results. The addition of FNAC may allow identification before surgery, of all patients with breast cancer[3]. The present study has shown that when FNAC is performed at the clinic and reported immediately, it is possible to select at the first visit those patients who require surgical excision. This has reduced the excision rate in patients with benign disease. Subsequent follow-up has shown that no patient who did not undergo excision biopsy had a malignancy.

The decrease in surgical excision rate in patients with benign disease occurred despite 14 per cent of patients with benign lesions electing to have the lump removed. No patient has subsequently returned to the breast clinic or any other surgical unit in this hospital requesting surgery. Therefore, the commonly held view that women wish to have a breast lump removed, even if there is evidence that it is benign, has been shown to be incorrect.

Acceptance of FNAC in the management of breast disease in Britain has been limited, principally because of lack of expertise in the aspiration technique and interpretation of cytological specimens[3]. The incidence of unsatisfactory specimens and false-positive reports have been the main problem[1–5,7,8,12,13]. There appears to be a close relationship between the number of unsatisfactory specimens obtained and the experience of the individual performing the aspiration[4,15]. It should be appreciated that many benign lesions contain few parenchymal cells: it is, thus, impossible to obtain cellular aspirates from these areas. If an experienced individual aspirates a lesion and stromal elements are aspirated then we accept this as a satisfactory but acellular aspirate. Following the initial assessment of our results with immediate reporting of FNAC[6] and recently published data on FNAC in over 1200 patients[3,4,14], we now consider benign and acellular smears as confirming benign disease and an open biopsy is not undertaken. Where an acellular aspirate is obtained from a clinically suspicious lesion, then either a repeat aspirate is performed or the lump is removed. Follow-up has confirmed that those with acellular aspirates and clinically benign lesions do not have malignancy. False positives usually occur during the learning phase of the cytologist[3]. There have been no false positives in this centre and, during the study period, no false negatives. The accuracy of immediate reporting in the clinic is shown by the amendment of only one report, from benign to suspicious, following examination of all aspirated material.

During the two periods, similar numbers of fibroadenomas were removed. The natural history of fibroadenomas is unknown, although it is always taught that they frequently increase in size. Some studies, however, suggest that they may get smaller and even disappear with time[15,16] and a clinical diagnosis of fibroadenoma may be incorrect in up to 50 per cent of instances[17]. Although a clinical fibroadenoma with benign cytology need not be routinely excised, the majority of patients in the present series with fibroadenomas wished them to be removed. As they can be excised through small cosmetic incisions under local anaesthetic, excision of cytologically confirmed fibroadenomas over 1 cm is in our view the most appropriate treatment.

The major reduction in surgical excision rate was due to far fewer biopsies being performed for 'fibrocystic disease'. One reason suggested for biopsy in this condition is that it allows identification of patients at increased risk of subsequent breast cancer[18]. Patients at risk are those with epithelial hyperplasia and atypia. Aspirates from these lesions are cellular and usually fall into the suspicious category[3]. Both patients in the present series with suspicious cytology were found to have epithelial hyperplasia on subsequent histological examination. As all patients with suspicious cytology undergo surgical excision, this group of patients should be identified by FNAC.

FNAC reported in the clinic allows immediate diagnosis of a breast lump and reduces the number of open biopsies in benign breast disease, and this has financial implications. During the second 3-month period studied it can be estimated that the use of FNAC resulted in 23 less breast biopsies. This has important implications in an area with limited resources. The major advantages of FNAC with immediate reporting, as practised in our clinic, are not financial, but are that this technique allows early reassurance and the avoidance of unnecessary surgery in patients with benign disease, while at the same time detecting all patients with breast cancer.

References

1. Zajicek J. *Aspiration Biopsy Cytology Part 1: Monographs in clinical cytology*. Basle: Karger, 1974.
2. Schöndorf H. *Aspiration Cytology of the Breast*. Philadelphia: Saunders, 1978.
3. Dixon JM, Anderson TJ, Lamb J, Nixon SJ, Forrest APM. Fine needle aspiration cytology, in relationship to clinical examination and mammography in the diagnosis of a solid breast mass. *Br J Surg* 1984; **71**: 593–6.
4. Dixon JM, Lamb J, Anderson TJ. Fine needle aspiration cytology of solid breast lumps: the importance of the aspirator. *Lancet* 1983; **ii**: 564.
5. Webb AJ. The diagnostic cytology of breast carcinoma. *Br J Surg* 1970; **57**: 259–64.
6. Dehn TCB, Clarke J, Dixon JM, Crucioli V, Greenall MG, Lee ECG. Fine needle aspiration cytology with immediate reporting in the outpatient diagnosis of breast disease. *Ann R Coll Surg Engl* 1987, in press.
7. Duguid HLD, Wood RAB, Irving AD, Preece PE, Cuschieri A. Needle aspiration of breast with immediate reporting of material. *Br Med J* 1979; **ii**: 185–7.
8. Thomas MJ, Fitzharris BM, Redding WH *et al.* Clinical examination, xeromammography and fine needle aspiration in the diagnosis of breast tumours. *Br Med J* 1978; **ii**: 1139–41.
9. Cahill CJ, Boulter PS, Gibbs NM, Price JC. Features of mammographically negative breast tumours. *Br J Surg* 1981; **68**: 882–4.
10. Dixon JM, Crofts TJ, Armstrong CP, Lee D, Wilson J, Forrest APM. The advantage of adrenaline in local and general anaesthetic breast biopsy. *J R Coll Surg Edinb* 1983; **28**: 292–4.
11. Bundred NJ, Dixon JM, Chetty U, Forrest APM. Mammillary fistula. *Br J Surg* 1987; **74**: 466–8.
12. Furnival CM, Hughes HE, Hocking MA, Reid MMW, Blumgart LM. Aspiration biopsy in breast cancer. *Lancet* 1975; **ii**: 446–8.
13. Davies CJ, Elston CW, Cotton RE, Blamey RW. Pre-operative diagnosis in carcinoma of the breast. *Br J Surg* 1977; **64**: 326–8.
14. Barrows GH, Anderson TJ, Lamb J, Dixon JM. Fine-needle aspiration of breast cancer: relationship of clinical factors to cytology results in 689 primary malignancies. *Cancer* 1986: **58**: 1493–8.
15. Kern WH, Clark RW. Retrogression of fibroadenomas of the breast. *Am J Surg* 1973; **126**: 59–62.
16. Furnival CM, Irwin JRM, Gray GM. Breast disease in young women—when is biopsy indicated? *Med J Aust* 1983; **2**: 167–9.
17. Wilkinson S, Forrest APM. Fibroadenoma of the breast. *Br J Surg* 1985; **72**: 838–40.
18. Dupont WD, Page DL. Risk factors for breast cancer in women with proliferative breast disease. *N Engl J Med* 1985; **312**: 146–51.

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Choice of surgery for early breast cancer: pre- and postoperative levels of clinical anxiety and depression in patients and their husbands

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Two groups of patients with early breast cancer were studied prospectively to assess whether being offered a choice of surgery (simple mastectomy or wide excision plus radiotherapy) influenced levels of anxiety and depression pre- and postoperatively. A significantly higher percentage of the patients not *offered a choice of surgery experienced high levels of anxiety and depression pre-operatively and up to 2 months postoperatively compared with patients offered a choice; the results were also similar for the husbands of these patients. At 4 months, differences between the two groups were not statistically significant, although the trend remained the same with more patients not offered a choice of treatment showing high levels of anxiety and depression. Patients offered a choice of surgery had similar pre- and postoperative levels of anxiety and depression to patients with benign breast disease and patients undergoing surgery for non-cancerous conditions.*

Keywords: Anxiety, depression, breast cancer, surgery

Five-year survival and disease-free intervals are equivalent following both simple mastectomy and wide excision plus radiotherapy for early breast cancer[1]. It has recently been suggested that patients should be allowed to choose between wide excision and mastectomy for breast cancer[2]. There are, however, few published data which indicate psychological outcome following choice of treatment, and even fewer regarding the impact breast cancer has on marital relationships from the husband's point of view. It is of course possible that being offered a choice may have negative outcomes; for example, patients might feel their doctor is uncertain how to treat the cancer and this may be deleterious to wellbeing.

The purpose of this pilot study was to record prospectively the pre- and postoperative psychological outcome of both patients and their husbands in order to ascertain the effect that patient choice of surgery has on pre- and postoperative adjustment.

Patients and methods

Thirty patients with early breast cancer (stage I or II) who attended the Royal South Hants breast clinic between October 1985 and April 1986 participated in the study. There were two groups of breast cancer patients matched for stage of disease and age: those offered a choice of surgery and those not offered a choice. As this was a pilot study, we did not feel it ethical to allocate patients to groups randomly. The two groups arose because patients with centrally located tumours were not offered a choice of surgery; at the time of this study it was the policy to perform mastectomy for centrally positioned tumours. Twenty patients were given a choice of operation, seven choosing mastectomy and thirteen choosing wide excision plus radiotherapy. Patients who chose mastectomy did so largely because they wanted the 'whole area containing the cancer' removed, or to avoid radiotherapy; those who chose wide excision did so to preserve the breast and to undergo a 'less drastic procedure'. The 10 patients not given a choice owing to the central position of the tumour underwent mastectomy; all patients had an axillary clearance. External beam radiotherapy for all the wide excision patients and three of the mastectomy patients was commenced approximately 4 weeks postoperatively and was given on 5 days a week for 5 weeks. Two groups of patients acted as controls: one group ($n=31$) with benign breast disease who did not undergo surgery, and a second group ($n=20$) of general surgical patients who had surgery for non-cancerous conditions such as varicose veins and gallstones.

Patients were told the diagnosis in the out-patients department by one of the consultants and, where relevant, the treatment options were outlined. A pre-operative diagnosis of breast cancer was made in all patients and was based upon results from three tests: cytology, mammography and clinical examination[3]. All patients were seen pre-operatively by a breast specialist nurse for further advice. Both groups were counselled by this nurse who took care to ensure that those patients not offered a choice of surgery were aware that this was due to the position of the tumour. Patients were admitted to hospital either 1 or 2 weeks after diagnosis which allowed them time to consider the options and have further consultations if necessary. The final decision was taken on the day before surgery.

All patients attending the breast clinic saw the interviewer (J.M.) on their first visit. Where a diagnosis of cancer was made, patients were asked if they would be willing to be interviewed upon admission to hospital; at this stage, no patients refused. Patients, and husbands if present, were seen on the ward on the day before surgery, and the nature of the project was explained. Thirty-one patients, aged under 70 years with no previous history of psychiatric illness, were approached and all but one agreed to participate; twenty-five were married, four were widowed and one was single.

Details of ages and numbers of patients and husbands in each group are shown in *Table 1*.

Levels of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale[4], self-esteem using the Rosenberg (1965) scale[5], and a general assessment of symptoms using the Rotterdam Symptom Checklist[6]. In addition to completing the above, patients were interviewed using a semi-structured interview schedule to assess the effect breast cancer has on social and work activities, and marital relationships. However, in this preliminary report, only the data obtained from the Hospital Anxiety and Depression Scale for the first three interviews are presented in detail. All patients were interviewed on the day before surgery and thereafter at 2-monthly intervals for 10–12 months. Husbands completed the questionnaires and the interview schedule on the day before surgery, 2, 6 and 10–12 months postoperatively. Patients in the control groups completed the questionnaires only; the benign disease group at 1 week, 6 months and 10 months post-diagnosis; and the general surgical group on the day before surgery, 6 months and 10 months postoperatively. It is hoped that further results will be published as they become available.

This work was presented at the Surgical Research Society meeting in January 1987.

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Table 1 *Ages of patients and husbands*

Group	Number: Patients	Number: Husbands	Age (years) Median (range): Patients	Age (years) Median (range): Husbands
Patient—choice	20	—		
Married	16	12*	49·5 (27–68)	49·0 (36–67)
Widowed	4	—		
Patient—no choice	10	—		
Married	9	7†	44·5 (38–61)	51·0 (38–59)
Single	1	—		
Benign breast disease	31	—	44·0 (28–65)	—
General surgical	20	—	39·5 (28–66)	—

* One husband did not wish to participate; three patients did not wish their husbands to be included in the study
† One husband did not wish to participate; one patient did not wish her husband to be included

Table 2 *Median scores from the self-esteem scale and the physical complaints subscale of the Rotterdam Symptom Checklist*

	Patients no choice 1	2	3*	Patients chose wide excision 1	2	3	Patients chose mastectomy 1	2	3
Self-esteem	29	30·5	33	30	30	30	32	32·5	34
Physical complaints	10	10·5	5	9	6	5	7	9·5	5

* 1 = pre-operative interview; 2 = 2 months postoperatively; 3 = 4 months postoperatively

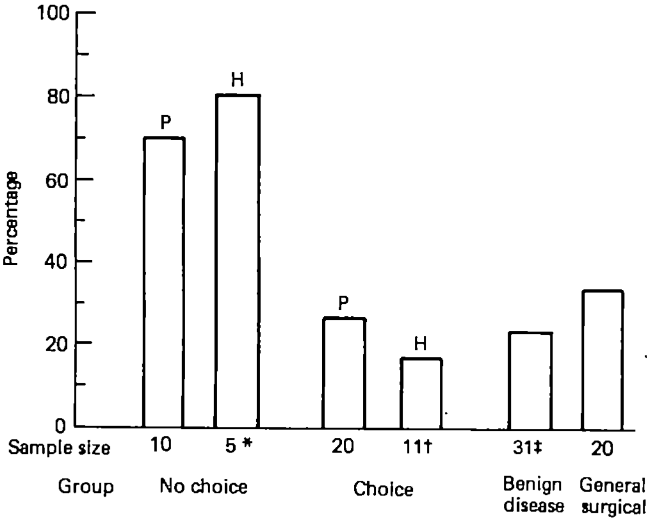

Figure 1 *Percentage of patients (P) and husbands (H) with clinical levels of anxiety pre-operatively. *Two failed to complete the questionnaire; †one failed to complete the questionnaire; ‡assessed 1 week after diagnosis*

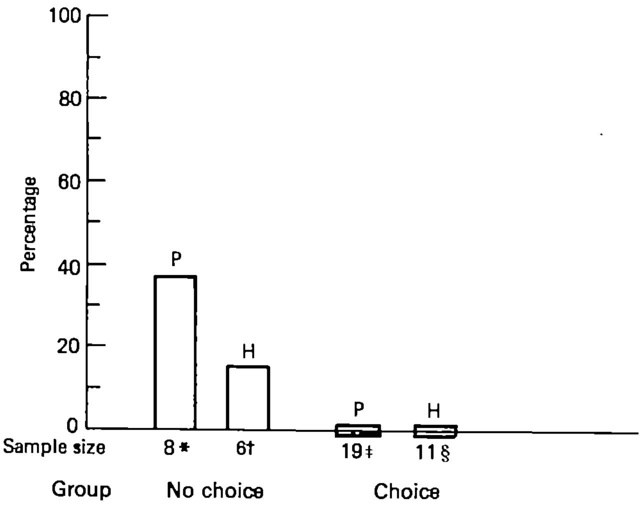

Figure 2 *Percentage of patients (P) and husbands (H) with clinical levels of anxiety 2 months postoperatively. *Two withdrew from the study; †one failed to complete the questionnaire; ‡one suffered a stroke and was withdrawn; § one withdrew from study*

Results

Data from the self-esteem scale and the physical complaints subscale of the Rotterdam Symptom Checklist were analysed using Kruskal–Wallis one-way analysis of variance by ranks. Scores from the self-esteem scale were derived from the original 10 items in the scale and may yield a maximum score of 40; the higher the score, the higher the sense of self-esteem. The physical complaints subscale comprised 21 items from the checklist and can result in a maximum score of 63; the higher the score, the more physical complaints reported. The results from the analyses revealed that there were no significant differences *between* the groups at the pre- and postoperative interviews, nor *within* groups. The median scores are presented in *Table 2*.

Figures 1–3 illustrate the percentage of patients and husbands with *clinical* levels of anxiety pre- and postoperatively, and *Figure 4* illustrates the *clinical* levels of depression pre-operatively; clinical levels reflect scores of 11 plus (maximum of 21) on each of the anxiety and depression subscales[4].

The data were analysed using a unified analysis of variance for ranks test[7].

The results show that a significantly higher percentage of patients and husbands *not* offered a choice of operation were clinically depressed and anxious pre-operatively compared with those given a choice ($P < 0{\cdot}05$, *Figures 1* and *4*). The trend was similar for both anxiety (*Figures 2* and *3*) and depression for the first two postoperative assessments, although the results only reached statistical significance ($P < 0{\cdot}05$) for the patient group at the first postoperative assessment. Of those who were offered a choice, there were no significant differences in levels of clinical anxiety or depression between those who chose mastectomy and those who chose wide excision plus radiotherapy. Patients given a choice of surgery had similar levels of anxiety and depression both pre- and postoperatively to patients with benign breast disease and patients undergoing general surgical operations for non-cancerous conditions.

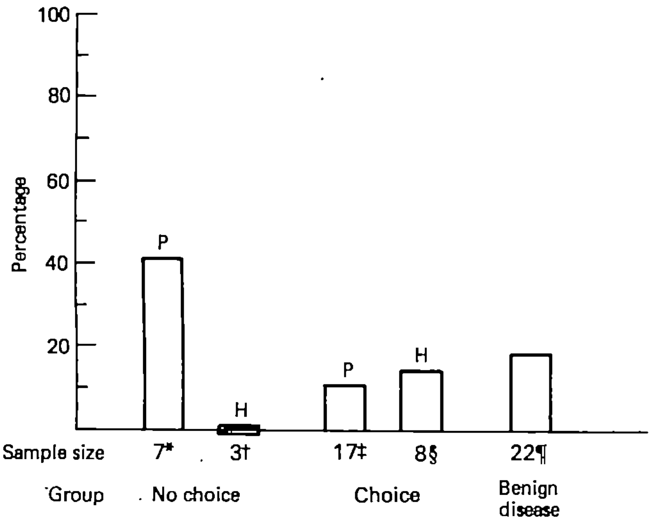

Figure 3 *Percentage of patients (P) and husbands (H) with clinical levels of anxiety at the second postoperative assessment (4 months for cancer patients; 6 months for husbands and patients with benign breast disease. (N.B. insufficient data available from the general surgical group.) *One not yet interviewed; † two discontinued, one not yet not interviewed; ‡ one died, one withdrew from the study; § two withdrew, one not yet interviewed; ¶ no reply from 9 patients*

Discussion

There is a difference between the two groups of breast cancer patients: those patients offered a choice of surgery and their husbands show less anxiety and depression than those not offered a choice. These results are at variance with those which reported[8] that patients *not* given a choice were *less* anxious pre-operatively than those given a choice and, furthermore, that there was no evidence of severe depression or anxiety in either group postoperatively. However, their pre-operative assessment combined the results from patients who completed tests on the day before surgery with those who completed them when first seen in the clinic. Consequently, it is unclear whether the latter group were aware of their diagnosis at the time of testing. Furthermore, the differences may be due to the small numbers of patients involved in both studies, and/or differences in the way in which patients were managed.

In the present study, it is not immediately obvious why the patients not offered a choice of surgery and their husbands should be more distressed pre- and postoperatively than others. The groups differ in more than one way and there may be four possible explanations for the results.

1. The results may be attributable to the effects of mastectomy. However, this may be discounted because there were no differences in anxiety and depression between those who chose mastectomy, and those who chose wide excision plus radiotherapy.

2. The results may be due to the factor which distinguished the two groups clinically: the position of the tumour. However, there is no evidence to suggest that this would affect levels of anxiety and depression.

3. The patients in the no choice group may have believed their disease to be more serious. However, both groups of patients were counselled by the breast specialist nurse who explained the rationale behind the decision for surgery for those patients not offered a choice. We believe, therefore, that this explanation is probably not the reason for the differences between the groups with regard to levels of anxiety and depression.

4. Offering a choice of operation may reduce distress. This is the most likely explanation as levels of anxiety and depression in the choice group are lower than those commonly reported in the literature[9]. Furthermore, levels of anxiety and depression are lower in those patients who chose mastectomy, compared with those mastectomy patients not given a choice of surgery.

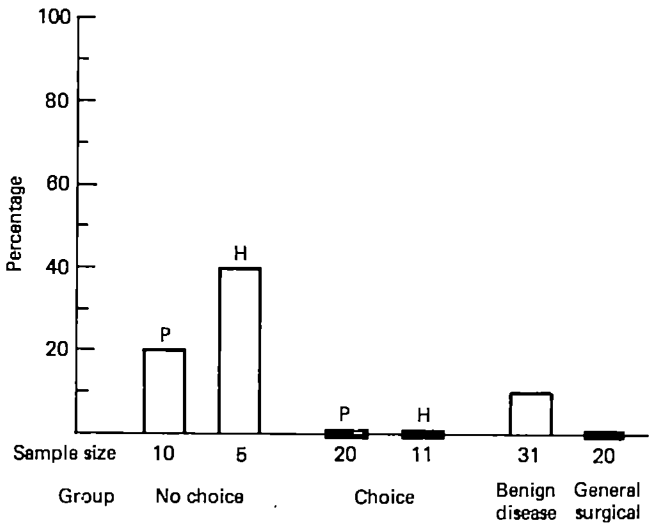

Figure 4 *Percentage of patients (P) and husbands (H) with clinical levels of depression pre-operatively*

In conclusion, we suggest that offering a choice of surgery does not appear to be doing any harm to patients, and may in fact reduce the levels of anxiety and depression commonly observed in breast cancer patients. However, offering patients a choice of surgery is not a simple matter. In our opinion, a choice should only be offered after counselling in conjunction with written information. Accordingly, we have produced an information leaflet outlining the two types of surgical procedure which reinforces what patients have been told in the out-patient clinic. Although the choice is generally in favour of wide excision plus radiotherapy, there may well be a minority of patients who will choose mastectomy. For those mastectomy patients who have not been offered a choice of surgery, it might aid postoperative adjustment if breast reconstruction is discussed at an early stage.

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References

1. Fisher B, Bauer M, Margolese R *et al.* Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *New Engl J Med* 1985; **312**: 665–73.
2. King's Fund Forum. Consensus development conference: treatment of primary breast cancer. *Br Med J* 1986; **293**: 946–7.
3. Smallwood J, Cuyer P, Dewsbury K *et al.* The accuracy of ultrasound in the diagnosis of breast cancer. *Ann R Coll Surg Engl* 1986; **68**: 19–22.
4. Zigmond A, Snaith R. The hospital anxiety and depression scale. *Acta Psych Scand* 1983; **67**: 361–70.
   Acta Psychiatrica Scandinavia 1983; **67**: 361–70.
5. Rosenberg M. *Society and the Adolescent Self Image.* New Jersey: Princeton University Press, 1965.
6. Trew M, Maguire P. Further comparisons of two instruments for measuring quality of life in cancer patients. *Proc Third EORTC Workshop of Quality of Life.* Paris. 1982.
7. Meddis R. *Statistics Using Ranks. A Unified Approach.* Oxford: Basil Blackwell Ltd, 1984.
8. Ashcroft J, Leinster S, Slade P. Mastectomy versus breast conservation: Psychological effects of patient choice of treatment. In: Watson M, Creer S, eds. *Psychological Issues in Malignant Disease.* Oxford: Pergamon Press, 1986: 55–71.
9. Maguire P. The psychological impact of cancer. *Br J Hosp Med* 1985; **34**: 100–3.

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Consultations for breast disease in general practice and hospital referral patterns

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As part of the evaluation of a health education campaign about breast disease, consultations for breast problems were monitored in five general practices over an 18-month period in Edinburgh. No increase was found as a result of the campaign, nor was there any increase in the number of biopsies performed. On average, each GP saw 13 women with breast problems each year, a rate of 1·6 per cent; 29 per cent were referred to hospital, regardless of their age. The most common presenting symptom was pain (47 per cent), with 35 per cent complaining of a lump. The reasons for hospital referral are discussed. It is suggested that GPs may refer too many young women to a specialist clinic, although this may be inevitable.

Keywords: GP referrals, breast

It is almost 10 years since Bywaters studied the incidence of breast disease in a general practice because of the 'possible introduction of breast cancer screening'[1]. The reality of such a screening service is now close[2], but there is little information on the current workload of breast disease for the GP or on whether screening programmes would increase the referral rate to hospital among women *not* offered screening because of their age. In a survey in 1983, we found that many GPs had already perceived an increase in consultations and requests for information about this subject[3]. This was particularly noted in Edinburgh, where a randomized trial of breast screening is in progress, involving 84 general practices[4]. Half the practices are offered screening for women aged 45–64, the other half acting as control practices in which case no screening is available. A health education campaign about breast disease and breast self-examination aiming to raise general awareness ran in parallel to the screening trial for 2 years from 1981 to 1983[5].

The aim of the study we report here was chiefly to determine whether the number of GP consultations for breast problems, or of surgical operations for breast disease, increased as a result of our health education campaign. In addition, we describe the workload of GPs in control practices that were not offered breast screening for their women although they may have had greater awareness and interest than women in other cities.

Methods

Doctors in control practices agreed to collaborate in a study to monitor all consultations for breast symptoms over an 18 month period, which included 6 months before and 12 months after the start of the health education campaign. A short questionnaire was completed for each patient, asking for information on age, symptoms, the GP's diagnosis, referral to hospital, and the practice of breast self-examination. Questionnaires were completed only for women who consulted primarily about their breasts: women who had a breast examination because of contraceptive advice or because they attended for a cervical smear were not included. The patient's identity was not recorded as permission for this had not been sought, so the final diagnosis in cases referred to hospital was not available to us. Although these practices were not offered screening, GPs in this study were allowed to refer a small number of women to the screening clinic for a single examination if appropriate. The indications explained to the GPs were as follows: a woman aged 45–65 could be referred if she wished to have screening, but had minimal or no symptoms and no clinical abnormality. In the event, over a third of women referred were below this age group. The questionnaires were collected regularly from the practices, coded and computerized. Analysis was done using the standard SPSS package.

The number of breast operations carried out in all Edinburgh hospitals from 1979 to 1984, both for benign and malignant disease of the breast, was obtained from the surgical audit figures[6].

Results

A total of 262 questionnaires were returned from five practices over an 18 month period. There was no indication of any increase in the rate of consultation, but there was a suggestion of a seasonal variation (*Figure 1*).

The number of biopsies for both benign and malignant disease of the breast from 1979 to 1984 is shown in *Figure 2*, together with an estimate of referrals to surgical outpatient

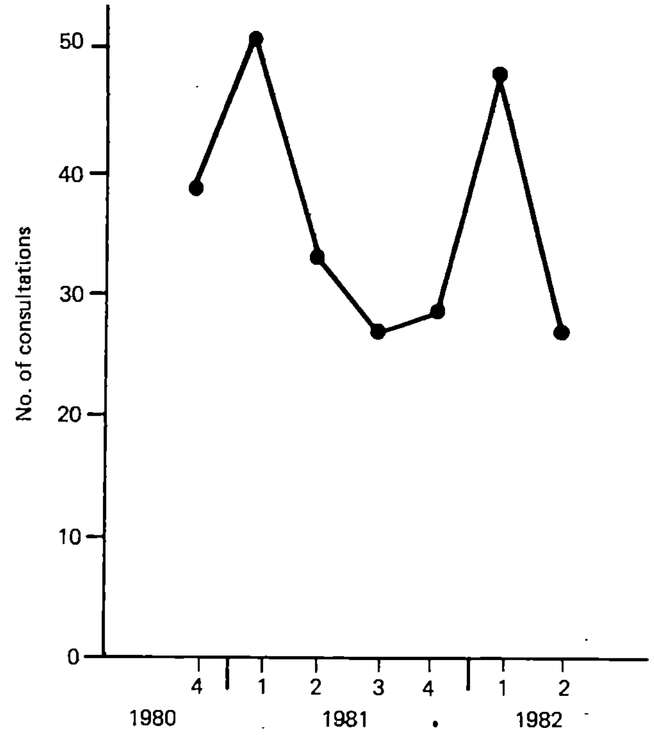

Figure 1 *The number of consultations for breast problems over 18 months in the five practices: period 1, January–March; period 2, April–June; period 3, July–September; period 4, October–December*

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clinics. The number of surgical procedures did not increase over a 7 year time period and there seems to be no major increase as a result of the health education programme. On the other hand, the estimated referral rate to hospital shows a substantial increase over the 7 years, most of it to the specialist breast clinic in the academic Department of Clinical Surgery. Altogether, referrals as a result of the breast screening trial accounted for about 10 per cent of the total biopsies performed.

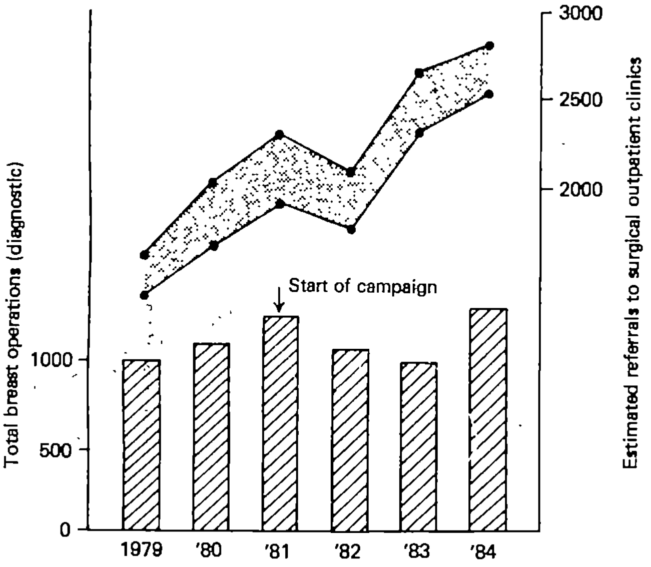

Figure 2 *The total number of diagnostic breast operations in Edinburgh hospitals from 1979–1984, and the estimated referrals to all surgical outpatient clinics over the same period (including the Breast Clinic in the Department of Clinical Surgery). Estimated referrals calculated as either the same proportion of biopsies done in other units as in the Department of Clinical Surgery (upper limit of shaded area), or on the basis that the other units biopsied all referred patients (lower limit of shaded area). The correct number of referrals lies somewhere between the two*

The incidence of breast problems according to the total number of women registered in each practice and in the age group 45–65 years was calculated (*Table 1*). The number of women in the age group 45–64 was known to us through our population register for the randomized trial of breast screening and the total number of women in each practice was obtained by request from the GPs. On average, 1·6 per cent of women consulted each year (1·8 per cent of women aged 45–64) and each GP saw 13 women annually.

The questionnaire data were analysed in terms of symptoms and outcome and the results are given in *Tables 2, 3* and *4*. From *Table 2* it can be seen that the most commonly recorded complaint was pain, even in older age groups, and nipple discharge was very rare. The proportion of women complaining of a lump, with or without pain, was highest in those under 34 years of age (52 per cent) and lowest in women aged 55–64 (only 10 per cent).

The diagnosis made by the GP and the outcome of the consultations are shown in *Table 3*. Cancer was suspected in only 9·5 per cent of cases and not necessarily in the older age group; as many as 27 per cent were thought to be normal, requiring only reassurance. A total of 29 per cent of women were referred to hospital and a further 22 per cent to the breast screening clinic. From the point of view of the screening trial, only 37 or 10 per cent of control women (aged 45–64) were referred to the clinic.

The referral to hospital according to the age group is shown in *Table 4*. There is no age-related pattern, except that a larger proportion of women aged over 65 were referred. Altogether, one-third of women under 35 years of age were referred to hospital. Of all women who presented with a lump as the main

Table 1 *Consultation rates in the practices*

Practice	Rate/GP per year	Rate/1000 women per year All ages	Age 45–65
A	18	17	19
B	9	19	17
C	13	13	16
D	16	*	13
E	10	*	27
Average	13	16	18

* Total number of women not known

Table 2 *Symptoms according to age group in the five practices*

Main symptom	Age <34	35–44	45–54	55–64	>65	All
Pain	37	31	30	20	6	124
Lump (±pain)	45	20	19	3	6	93
Discharge	1	1	1	0	0	3
Other	4	11	12	7	1	35
Total	87	63	62	30	13	255*
Percentage with lump as symptom	52%	32%	31%	10%	46%	36%

* Missing data in seven questionnaires

Table 3 *GP diagnosis related to symptoms and outcome of consultations*

	Pain (124)	Lump (93)	Nipple discharge (3)	Other (40)	All (262)
Suspected diagnosis					
Cancer	3	7	0	0	10 (9·5%)
Unknown mass	2	12	1	0	15
Benign	51	45	—	5	101 (38·5%)
Normal (including anxiety)	39	13	2	18	72 (27·5%)
Other	22	12	—	17	51 (19·5%)
Outcome					
Hospital referral	21	47	1	6	75 (29%)
Clinic	33	16	2	13	57 (22%)
Reassurance	54	24	—	19	97 (37%)
Other	11	3	—	—	14 (5%)

Items of data were missing from 7 per cent of the returned questionnaires, so the groups do not necessarily add up to 100 per cent

Table 4 *Referral to hospital according to age group*

	Age					
	<24	25–34	35–44	45–54	55–64	>65
Total	32	55	63	62	35	13
Referral to hospital	11 (34%)	19 (35%)	17 (27%)	20 (32%)	4 (11%)	6 (46%)
Referral to clinic	3 (10%)	10 (18%)	10 (15%)	21 (33%)	16 (45%)	2 (16%)
Total referrals (%)	44%	53%	42%	65%	56%	62%
Percentage complaining of lump who were referred to hospital	41%	54%	55%	47%	33%	67%

symptom, half were referred to hospital and this bore no relation to age.

From the questionnaire, 33 per cent of women had come across recent publicity (not necessarily our health education programme) about breast disease, and 21 per cent of women said this had influenced their attendance at the GP. When asked if they had ever carried out breast self-examination, 61 per cent of women said they had. Their source of knowledge about breast disease was mainly through the media (46 per cent) or a variety of health professional sources (23 per cent). Only 8 per cent had learned through their GP.

Discussion

It seems there was no impact of the health education campaign on GP consultation rates. Interestingly, this was also found in the Southampton study, which was carried out after 1 month of intensive health education campaigning[7]. Although such campaigns may appear to have little measurable effect on consultation rates, this could also mean that they do not lead to the raised anxiety levels in women as some have feared.

Our study was carried out over a long period, and it is possible that an increase in consultation rates is masked by a fall-off in returning the questionnaires. However, the GPs all said they had not noted any particular increase. It is a criticism of our study design that the time period was long, making it more difficult to sustain interest. We tried to overcome this by making regular visits to the practices.

There was a steady increase in the number of biopsies and referrals to the diagnostic (hospital-based) breast clinic over a period of 6 years. The reasons for this are probably that local GPs have made increasing use of the facilities provided. There has also been a marked increase in patients referred from outside the city as the clinic became more well-known. Interestingly, there is no corresponding increase in biopsy rates, but these are complicated by hospital strikes during this period and an increasing use of fine needle aspiration cytology. Hospital biopsy rates are complex and will be the subject of a further paper, including an assessment of the contribution from screening.

The number of women seen with breast problems each year by the GP was similar to that found by Bywaters 10 years ago[1]. Altogether, 35 per cent of women attended their GP because of a lump and 47 per cent because of pain. These figures are very similar to those found in the Southampton study, which were 36 per cent and 52 per cent respectively[8]. We were surprised by the low proportion of women in the age group 55–64 who presented with a lump and have no particular explanation to offer. It may be related to the end of the menopause.

Although there was suspicion of cancer in just under 10 per cent of all women, 29 per cent were referred to hospital and 22 per cent to the screening clinic. On the other hand, the GP was able to reassure 37 per cent of women. In Southampton, 25 per cent were referred to hospital and 40 per cent were reassured. The control GPs in Edinburgh have co-operated well in not using the screening clinic during the trial, but once screening becomes generally available, it will be important to know the level of demand outside the designated age group of 50–64 years[2], and its bearing on the surgical services. There will inevitably be a small increase in the number of biopsies performed as a result of screening.

It is of note that the proportion of young women referred to hospital was similar to that in older women, yet the risk of breast cancer is very low in young women and rises steeply with increasing age. This is interesting and poses the question: Why does the GP worry as much about young women as about old? It may be that young women are more likely to request specialist advice and frequently their breasts are difficult to examine[10].

It remains to be seen whether new screening programmes and possible increased publicity will cause a major increase in the workload of the GP and the surgeon in relation to breast symptoms.

Acknowledgements

We acknowledge with gratitude the work of the GPs who made this study possible. We are also very grateful to the Surgical Audit Group who made available the figures relating to biopsy, to the Scottish Cancer Registry for incidence and registration data and to Professor Sir Patrick Forrest, Mr U. Chetty and surgical colleagues for permission to quote breast clinic figures. This study was funded by the Cancer Research Campaign, by a grant to one of us (M.M.R., Grant No. SP1575).

References

1. Bywaters JL. The incidence and management of breast disease in a general practice. *J R Coll Gen Pract* 1977; **27**: 353–7.
2. *Breast Cancer Screening.* The report to the Health Ministers of England, Wales, Scotland and Northern Ireland by a Working Group chaired by Professor Sir Patrick Forrest (1987).
3. Kalache A, Roberts MM, Stratton I. Breast cancer: views of general practitioners on its detection and management. *J R Coll Gen Pract* 1984; **34**: 250–4.
4. Roberts MM, Alexander FE, Anderson TJ *et al.* The Edinburgh randomized trial of screening for breast cancer: description of method. *Br J Cancer* 1984; **50**: 1–6.
5. Roberts MM, Robinson SE, French K, Elton RA, Talbot H. The Edinburgh Breast Education Campaign on breast cancer and breast self-examination: was it worthwhile? *J Epidemiol Community Health* 1986; **40**(4): 338–43.
6. Surgical Audit Group. By kind permission of the Chairman and Secretary, Edinburgh City Hospitals.
7. Nichols S, Waters WE. The effect of health education intervention about breast cancer amongst general practitioners on speed of referral and outpatient workload. *Community Med* 1984; **6**: 115–18.
8. Nichols S, Waters WE, Wheeler MJ. Management of female breast disease by Southampton General Practitioners. *Br Med J* 1980; **281**: 1450–3.
9. Holmberg L, Adami HO, Persson I, Lundstrom T, Tabar L. Demands on surgical inpatient services after mass mammographic screening. *Br Med J* 1986; **293**: 779–82.
10. Roberts MM, Adams S. Breast cancer and benign breast disease. In: McPherson A, Anderson A, eds. *Women's Problems in General Practice.* Oxford University Press, 1987: 94–106.

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Prognostic factors related to survival and groin recurrence following therapeutic lymph node dissection for lower limb malignant melanoma

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A retrospective analysis was carried out of 133 patients undergoing therapeutic lymph node dissection for malignant melanoma of the lower limb. A radical ilio-obturator dissection (RID) was performed in 106 patients and a superficial femoral dissection (SFD) in the remaining 27. On univariate analysis five factors were found to be significant indicators of prognosis. These were: Clark level of the primary ($\mathrm{P}=0{\cdot}02$); primary melanoma thickness ($\mathrm{P}=0{\cdot}04$); total number of positive nodes ($\mathrm{P}<0{\cdot}001$); number of positive femoral nodes ($\mathrm{P}<0{\cdot}001$); and number of positive ilio-obturator nodes ($\mathrm{P}<0{\cdot}001$). On multiple regression analysis only the number of positive nodes in each compartment remained a significant independent factor ($\mathrm{P}<0{\cdot}001$). The morbidity associated with RID was not significantly greater than after SFD. RID was, however, associated with a reduction in subsequent groin recurrence. Radical nodal clearance is the operation of choice. This technique provides maximum prognostic information, reduces the likelihood of local untreatable disease and possibly improves overall survival rates—especially when only one iliac node is involved.

Keywords: Melanoma, prognosis, survival, local recurrence, therapeutic dissection, complications

The management of adult solid cancers traditionally relied on excision of the primary tumour and the draining lymph nodes. Nodal metastases were thought to have a *controlling* influence on prognosis. Recently, it has been emphasized that nodal metastases are *indicators*, not governors of survival[1]. The variable use of regional lymph node block dissection in the management of malignant melanoma highlights this change in philosophy[2]. Once lymph nodes become clinically positive, the most important prognostic indicator appears to be the extent of nodal metastases[3–10]. However, the extent of surgical lymphadenectomy has yet to be standardized. Some authors complete a radical ilio-obturator dissection (RID)[11], claiming there is therapeutic value in removing involved ilio-obturator nodes without any significant increase in morbidity[12,13]. Others advocate superficial femoral dissection (SFD).

The true value of groin dissection is difficult to determine as many series grouped together results for lower limb primaries with those for trunk primaries and where the site of the primary was unknown[3–10]. Moreover, most analysed the results of block dissection of the groin with those of the axilla and the neck. In addition, little discussion has centred on the extent of lymphadenectomy.

We studied a homogeneous group of patients with lower limb melanomas who developed lymph node metastases in the groin, in order to determine which prognostic variables significantly predict improved survival and to compare the morbidity following RID with that after SFD.

Patients and methods

The study group of 133 patients was obtained by a retrospective review of patients undergoing therapeutic lymph node dissection of the groin for lower limb melanomas presenting to two institutions. These included 89 patients under the care of G.W. at Westminster Hospital from 1960 to 1980 and 44 patients from the Royal Marsden Hospital from 1960 to 1983. Excluded from this series were: patients having prophylactic lymphadenectomy; patients with groin metastases from truncal primaries; and those where the site of the primary was unknown.

The following features were recorded: age and sex of the patient; original clinical stage; site, Clark level and thickness (mm) of the primary melanoma; the disease-free interval; operative technique; total number of positive nodes and the number of positive nodes in the femoral and the ilio-obturator compartments. The incidence of postoperative complications and groin recurrence was detailed. Survival was calculated from the time of lymphadenectomy. The prognostic significance of each of the above factors was analysed using the log rank and log rank trend tests. To assess the prognostic significance of the factors independent of one another a Cox multiple regression analysis was also performed[14]. Complication rates after different surgical procedures were analysed using the χ^2 method.

In the Westminster series, RID was carried out in 76 patients and a SFD was performed in the remaining 13 cases. The Royal Marsden patients were under the care of two surgical oncologists (G.W. and H.W.). Thirty patients had an RID and fourteen a SFD. Of the latter group, six were referred with ilac node recurrence having had a SFD carried out at another hospital.

The median follow-up period was 102 months (range 6–276 months). To date, 79 (59·4 per cent) of the patients have died.

Results

The mean age at the time of lymphadenectomy was 48 years (range 17–72 years). Ninety-two patients were women (69·2 per cent).

Fifteen per cent presented with synchronous primary melanoma plus clinically involved groin lymph nodes; the remainder developed metachronous nodal metastases. Thirty-three melanomas (24·8 per cent) were located on the foot,

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Based on presentations to the British Association of Surgical Oncology, London, December 1984 and the Surgical Research Society, London, January 1985

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50·4 per cent on the leg and 24·8 per cent on the thigh. The distribution of Clark levels was 2·2, 38·7, 38·7 and 20·4 per cent respectively for levels II, III, IV and V, and tumour thickness was <2 mm in 13·6 per cent, 2–4 mm in 38·3 per cent and >4 mm in 48·1 per cent. Information regarding Clark level and tumour thickness was not available on 31·6 and 40·6 per cent respectively. These patients had presented before the introduction of microstaging and their pathological specimens were not available for review.

The disease-free interval between excision of the primary and the therapeutic lymph node dissection was 0 years in 15 per cent, <2 years in 57·1 per cent, 2–4 years in 14·3 per cent and >4 years in 13·6 per cent. RID was carried out in 106 patients (79·7 per cent) using the technique described by Westbury[11]. The remaining 27 patients (20·3) per cent) had a SFD. The number of positive lymph nodes in the femoral and ilio-obturator compartments is shown in *Table 1*. In the femoral compartment, 26 per cent of the patients had a single positive node, while 30 per cent had four or more involved nodes. In the ilio-obturator compartment 56 per cent of the patients had no metastases and 12 per cent had a single positive node. Two out of the one hundred and six patients having a RID had skip metastases to the ilio-obturator compartment with negative femoral nodes.

Survival

Using univariate statistics, survival was significantly related to: Clark level (*Figure 1*: $P=0{\cdot}02$); tumour thickness (*Figure 2*: $P=0{\cdot}04$); total number of positive nodes (*Figure 3*: $P<0{\cdot}001$); number of positive femoral nodes (*Figure 4*: $P<0{\cdot}001$); and the number of positive ilio-obturator nodes (*Figure 5*: $P<0{\cdot}001$). Age, sex, original clinical stage, site, disease-free interval, and type of operation did not significantly affect survival. Using the multiple regression model only the total number of positive nodes and the number positive in each compartment remained as significant independent prognostic variables ($P<0{\cdot}001$ in each case). Five-year survival rates and median duration of survival according to the number of positive nodes is shown in *Table 2*.

Table 1 *Number of positive nodes in each compartment*

Positive nodes	Femoral compartment ($n=133$)	Ilio-obturator compartment ($n=106$)	Overall ($n=133$)
0	2 (2)	59 (56)	0
1	34 (26)	13 (12)	33 (25)
2	26 (20)	22 (21)	16 (12)
3	31 (23)	11 (10)	24 (18)
4 or more	40 (30)	1 (1)	60 (45)

Values in parentheses are percentages

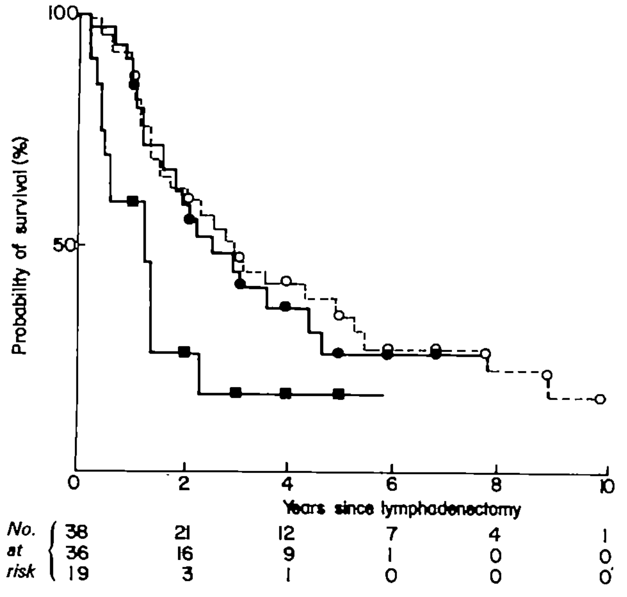

Figure 1 *Survival related to Clark level of invasion (total number of patients, 93)* ○------○ *Level 2 and 3 (38)*, ●——● *Level 4 (36)*, ■——■ *Level 5 (19)*, P=*0·02 (trend)*

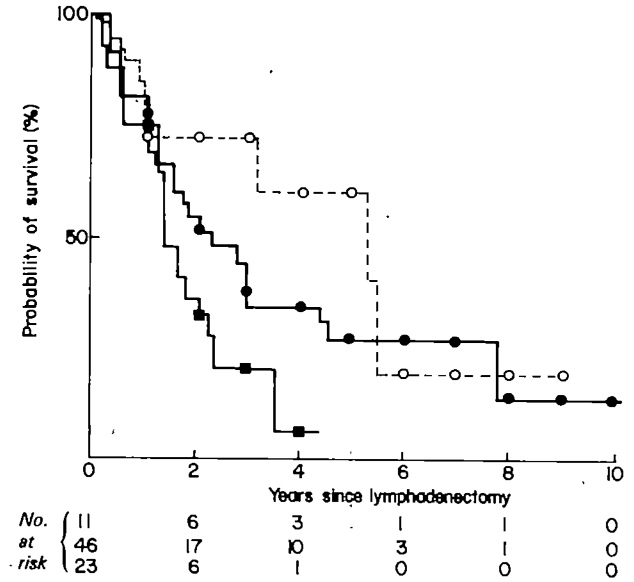

Figure 2 *Survival related to thickness of melanoma (total number of patients, 80)* ○------○ *<2 mm (11)*, ●——● *2–4 mm (46)*, ■——■ *>4 mm (23)*, P=*0·04 (trend)*

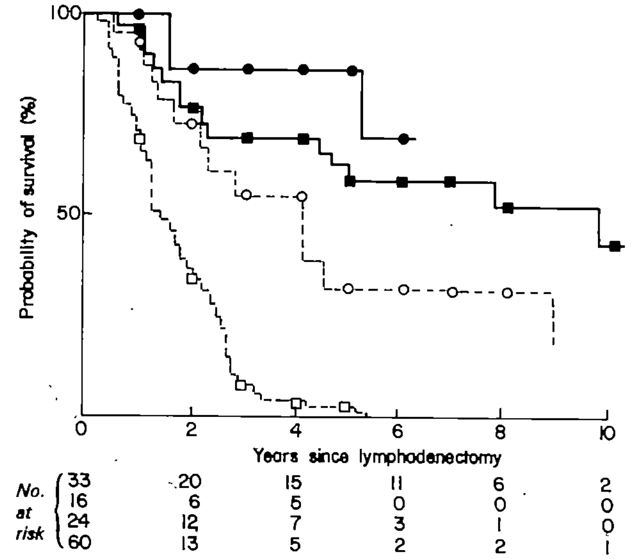

Figure 3 *Survival related to the total number of positive nodes (total number of patients, 133)* ■——■ *1 positive node (33)*, ●——● *2 positive nodes (16)*, ○------○ *3 positive nodes (24)*, □——□ *>4 positive nodes (60)*, P*<0·001 (trend)*

Sixteen patients survived for more than 6 years after lymphadenectomy, and three of these had one positive ilio-obturator node.

One of the patients with skip metastases to the ilio-obturator group had a thigh primary, a disease-free interval of 69 months and had a single positive node, the other had a foot primary, a disease-free interval of 73 months and had two positive nodes. After RID both are free of further disease 6 and 17 months later respectively.

Postoperative complications

One 73-year-old woman with five positive nodes died from bronchopneumonia 32 days after SFD.

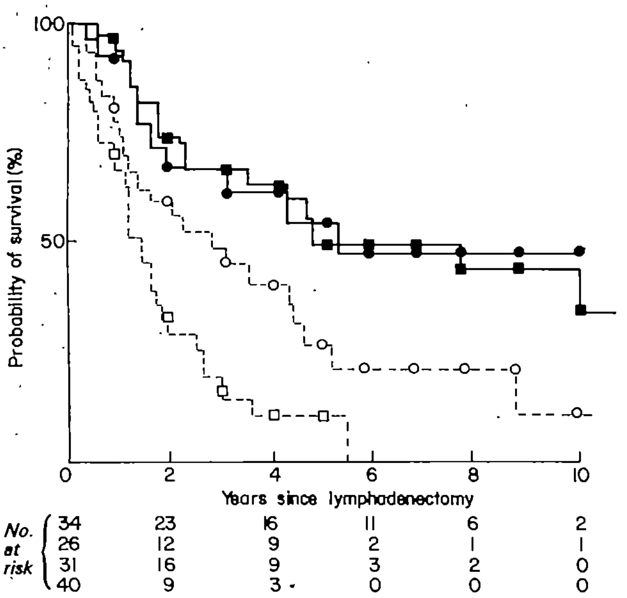

Figure 4 *Survival related to the number of positive superficial nodes (total number of patients, 131)* ■——■ *1 positive node (34),* ●——● *2 positive nodes (26),* ○------○ *3 positive nodes (31),* □------□ *>4 positive nodes (40),* P<*0·001 (trend)*

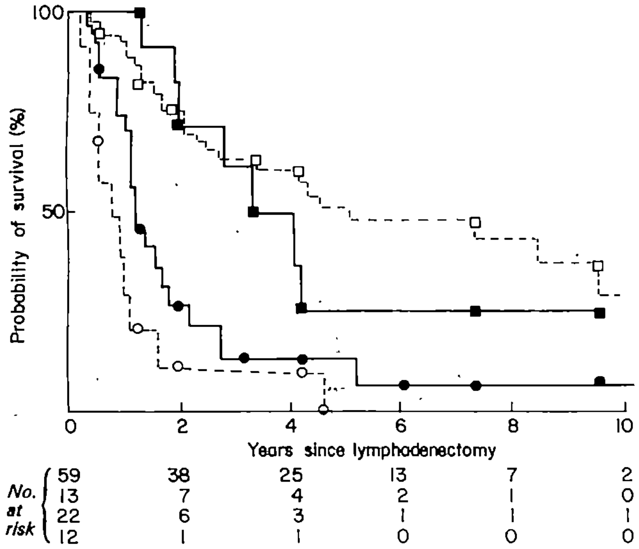

Figure 5 *Survival related to the number of positive ilio-obturator nodes (total number of patients, 106)* □------□ *negative nodes (59),* ■——■ *1 positive node (13),* ●——● *2 positive nodes (22),* ○------○ *>3 positive nodes (12),* P<*0·001 (trend)*

The recorded incidence of early and late complications is shown in *Table 3*. None of the differences in complication rates between the two operations was statistically significant, although the percentage of patients with each complication was greater following RID. Similarly there was no difference in the duration of hospitalization (mean duration in the RID group was 17·4 days ± 6·1 compared with 17·1 days ± 7·9 in the SFD group).

Groin recurrence

This was only assessed in the Royal Marsden series and occurred in 15 patients (34·1 per cent). Twelve of these have died and no patient has survived for 2 years. Groin recurrence was more frequent after SFD (57·1 per cent) than after RID (23·3 per cent) ($P<0·01$: log rank test), and was significantly related to the number of involved nodes ($P<0·005$). Six patients were referred with groin recurrence having had a SFD carried out elsewhere. In two instances, a salvage RID was performed, but in four cases the groin disease was fixed and untreatable by conventional means.

Discussion

In malignant melanoma, regional node metastases are the site of first relapse in 40 to 60 per cent of patients with recurring disease[15]. Previous reports have demonstrated that prognosis is related to certain features of the nodal metastases and others of the primary tumour. The most important prognostic indicator after univariate analysis appears to be the extent of nodal metastases. Thus, decreased survival has been reported when more than one[3-5], two[6,7], three [8,9] or more than 20 per cent of nodes are involved[10] and also when perilymph node invasion is seen[9]. Significant factors associated with the primary tumour are; thickness[7,8,16]; Clark level[7,16]; ulceration[4,8]; histogenetic type[7]; site[3,9]; and original clinical stage[7,16,17]. Our results concur with these findings. Only three papers (including the present study) carried out a multivariate analysis, and in each the features of the involved nodes assumed prime importance[7,8]. Differences in the above reports result from variations in the patients under study. For instance, Cascinelli *et al.* found that 56·5 per cent of their patients had one to two positive nodes[7] whereas in the present study this occurred in only 36·8 per cent. However, 30 per cent of their cases had prophylactic lymphadenectomy whereas all our patients had therapeutic lymphadenectomy. The present study is the first to confine itself solely to patients with clinically obvious groin metastases originating from leg melanomas.

Overall survival after nodal metastasis has been variously estimated as 28 to 42 per cent at 5 years and 15 to 42 per cent at 10 years[1]. Cascinelli *et al.* reported a 10-year survival of 43 per cent when one node was involved falling to 26 per cent when three were positive[7]. Our findings are similar (*Table 2*). In addition we found that the 5-year survival was 45 per cent when the ilio-obturator nodes were negative falling to 25, 14 and 0 per cent when one, two or more positive nodes were found in the upper compartment. These findings are in agreement with those of Finck *et al.*[17].

Table 2 *Five-year and median survival according to number of positive nodes*

	Percentage 5-year survival (95% confidence limits)	Median survival (months)
Total number of positive nodes		
1	55 (36, 72)	90
2	67 (30, 90)	78
3	31 (11, 56)	49
4 or more	2 (0, 5)	15
Number of positive iliac nodes		
0	45 (32, 60)	53
1	25 (5, 53)	42
2	14 (5, 32)	14
3 or more	0 (—)	9

Table 3 *Postoperative complications*

Complication	RID ($n=106$)	SFD ($n=27$)
Wound infection	21 (20)	2 (7)
Partial wound slough	24 (23)	3 (11)
Seroma	27 (26)	5 (19)
Clinical lymphoedema*	30 (28)	7 (26)
None	64 (60)	20 (74)

RID, radical ilio-obturator dissection; SFD, superficial femoral dissection. * Symptomatic or observable lymphoedema as recorded in the notes. Owing to the retrospective nature of this study, complications recorded in the notes may have been underestimated. Values in parentheses are percentages

Median survival after nodal metastases varies from 24 to 30 months after lymphadenectomy[7,8,16]. Callery *et al.* noted that median survival was 42 months when one to three nodes were involved but only 18 months when four or more were positive[8]. Finck *et al.* reported a median survival of 52 months when iliac nodes were negative falling to 20 months when positive[17]. In addition, Dasmahapatra and Karakousis noted that median survival with one positive node after RID was 41 months compared with 21 months when one positive node was found following SFD[13].

Wound related complications occur in 30–65 per cent following RID[3,12,13,18], compared with 7–30 per cent after SFD[13,19]. Seroma occurs in 24–29 per cent of patients following RID[13,18] compared with 18–23 per cent after SFD[13,19]. Lymphoedema occurs in 35–50 per cent following RID[12,13,18] compared with 26–30 per cent after SFD[13,19,20]. Our complication rates fall within these ranges. Because of the retrospective nature of this study the true complication rate may be considerably higher. No study has demonstrated statistically significant excess morbidity of RID when compared with SFD.

Groin recurrence occurs in 9–12·9 per cent of patients following RID[3,18]. We found that groin recurrence was significantly greater after SFD when compared with RID. This may result from selection bias, as many of these recurrences were specifically referred with the problem of uncontrollable disease following SFD. Irrespective of the operative procedure groin recurrence is an event of grave prognostic significance.

This study confirms that for patients with involvement of groin nodes, the extent of nodal metastases is the prime predictor of survival. Maximum prognostic information is obtained by carrying out RID. This technique is not accompanied by significant excess morbidity and confers greater palliative benefit than SFD in terms of regional control. Although we were unable to demonstrate any statistical survival advantage of RID over SFD, we found some circumstantial evidence suggesting that a radical dissection may so do. Thus, though 44·4 per cent of the ilio-obturator compartments contained positive lymph nodes, some patients with only one or two positive ilio-obturator nodes are long-term survivors following radical dissection (though there is no way of providing matched controls). In fact, of 16 of our patients surviving for more than 6 years, 3 had positive ilio-obturator nodes.

Whilst acknowledging the deficiencies of a retrospective study, we feel justified in concluding that RID is the treatment of choice for melanoma of the groin originating from a leg primary. This procedure provides accurate prognostic information, avoids untreatable regional disease in some patients, and may confer occasional survival benefit. In other words, for melanoma, lymph node metastases may be both *indicators* and *governors* of survival. Ultimately, these assumptions can only be resolved by conducting a prospective randomized trial of RID *versus* SFD.

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References

1. Cady B. Lymph node metastases. Indicators, but not governors o survival. *Arch Surg* 1984; **119**: 1067–72.
2. Day CL, Lew RA. Malignant melanoma prognostic factors 7 Elective lymph node dissection. *J Dermatol Surg Oncol* 1985; **11** 233–9.
3. Fortner JG, Booher RJ, Pack GT. Results of groin dissection for malignant melanoma in 220 patients. *Surgery* 1964; **55**: 485–94
4. Balch CM, Soong SJ, Murad T *et al.* A multifactorial analysis of melanoma III. Prognostic factors in melanoma patients with lymph node metastases (stage III). *Ann Surg* 1981; **193**: 377–88
5. Raynor CR. The results of node resection for clinically enlarged lymph nodes in malignant melanoma. *Br J Plast Surg* 1981; **34**: 152–6.
6. Karakousis CP, Seediq MK, Moore R. Prognostic value of lymph node dissection in malignant melanoma. *Arch Surg* 1980; **115**: 719–22.
7. Cascinelli N, Vaglini M, Nava M *et al.* Prognosis of skin melanoma with regional node metastases (stage II). *J Surg Oncol* 1984; **25**: 240–7.
8. Callery C, Cochran AJ, Roe DJ *et al.* Factors prognostic for survival in patients with malignant melanoma spread to the regional lymph nodes. *Ann Surg* 1982; **196**; 69–75.
9. Cohen MH, Ketcham AS *et al.* Prognostic factors in patients undergoing lymphadenectomy for malignant melanoma. *Ann Surg* 1977; **186**: 635–42.
10. Day CL, Sober AJ, Kopf AW *et al.* A prognostic model for clinical stage I melanoma of the lower extremity. Location on foot as independent risk factor for recurrent disease. *Surgery* 1981; **89**: 599–603.
11. Westbury G. Axillary and inguinal node clearance. In: Rob C, Smith R, eds. *Operative Surgery* 3rd edition. London: Butterworths, 1980: 433–8.
12. James JH. Lymphoedema following ilio-inguinal lymph node dissection. *Scand J Plast Reconstr Surg* 1982; **16**: 167–71.
13. Dasmahapatra KS, Karakousis CP. Therapeutic groin dissection in malignant melanoma. *Surg Gynecol Obstet* 1983; **156**: 21–3.
14. Cox DR. Regression models and life tables. *J R Stat Soc* 1972; **34**: 187–220.
15. Lee Y-T N. Loco-regional recurrent melanoma: 1 natural history. *Cancer Treat Rev* 1980; **7**: 59–72.
16. Roses DF, Provet JA, Harris MN, Gumport SL, Dubin N. Prognosis of patients with pathologic stage II cutaneous malignant melanoma. *Ann Surg* 1985; **210**: 103–7.
17. Finck SJ, Giuliano AE, Mann BD, Morton DL. Results of ilioinguinal dissection for stage II melanoma. *Ann Surg* 1982; **196**: 180–6.
18. Bowsher WG, Taylor BA, Hughes LE. Morbidity, mortality and local recurrence following regional node dissection for melanoma. *Br J Surg* 1986; **73**: 906–8.
19. Urist MM, Maddox WA, Kennedy JE, Balch CM. Patient risk factors and surgical morbidity after regional lymphadenectomy in 204 melanoma patients. *Cancer* 1983; **51**: 2152–6.
20. Sim FH, Taylor WF, Ivins JC, Pritchard DJ, Soule EH. A prospective randomized study of the efficacy of routine elective lymphadenectomy in the management of malignant melanoma. *Cancer* 1978; **41**: 948–56.

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Changes in the plasma sodium concentration after minor, moderate and major surgery

The plasma sodium concentration, $[Na]_P$, falls following major surgery and this fall is exacerbated by the administration of sodium-free or sodium-low intravenous fluids in the postoperative period. As a prelude to prospective, but controlled, studies we observed the range of $[Na]_P$ on admission for surgery in 477 patients. In 309 patients the extent of the change in $[Na]_P$ by the first postoperative day ($\Delta[Na]$) was related to the severity of the operation undergone (minor, moderate or major) and the volume of potentially hypo-osmolar intravenous fluid given. The mean admission $[Na]_P$ was significantly lower with increasing severity of proposed operation. A highly significant fall occurred in $[Na]_P$ following surgery of every grade; such falls in $[Na]_P$ were seen even when no potentially hypo-osmolar fluids were administered. A significant inverse relationship between admission $[Na]_P$ and $\Delta[Na]$ was demonstrated. We conclude that $[Na]_P$ falls following surgery of any severity and that such falls occur even when exogenous dilution cannot be implicated as a cause.

Keywords: Sodium, hyponatraemia

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Patients admitted to surgical wards often have plasma urea and electrolyte concentrations determined before and after surgery. A fall in plasma sodium concentration ($[\mathrm{Na}]_P$), often to hyponatraemic levels, is well known to occur after trauma and major surgery and the mechanism of this fall has been the subject of considerable study. It is widely believed that the fall in $[\mathrm{Na}]_P$ after uncomplicated surgery results from exogenous dilution, but this is often insufficient to cause all of the observed change[1]. In patients severely ill after operation profound falls in $[\mathrm{Na}]_P$ may occur and osmolal gaps are seen[2–7]. Low $[\mathrm{Na}]_P$ levels are also common in severely ill patients with a variety of non-surgical conditions[7–10]. Lowering of $[\mathrm{Na}]_P$ may be abrupt, or insidious and sustained. Abrupt falls in $[\mathrm{Na}]_P$ are often accompanied by osmolal gaps that are both dynamic and changing[7,8,10]. Sustained falls in $[\mathrm{Na}]_P$ are accompanied by reduced osmolality. The sick cell concept attributes osmolal gaps to isosmotic redistribution of solute, from cells to extracellular fluids, caused by an abrupt increase in cell membrane permeability; sustained dilution with no osmolal gaps to a widespread impaired capability of cells to maintain their normal content of non-diffusible solutes[7,8,10]. We are not aware of any work in which the early postoperative change in $[\mathrm{Na}]_P$ has been related to varying degrees of surgical trauma. The purpose of this study was, by observing all admissions to a surgical unit in a 9 month period, to quantify first the prevalence of hyponatraemia on admission and second the early postoperative change in $[\mathrm{Na}]_P$; and to relate both to the severity of the operation undertaken and the volume of hypo-osmolar fluid administered. The information obtained could then be used to select groups of patients or conditions for more detailed prospective study.

Patients and methods

During a 9 month period all patients admitted to a general surgical unit of 46 beds for elective or emergency surgery were studied. Patients who were not subsequently operated on were excluded. Venous blood was drawn for determination of plasma electrolyte levels pre-operatively and again on the first postoperative day at the discretion of the resident medical staff. The study was conducted using such routine sampling only, with no attempt being made to influence the decision as to whether or not to take a blood sample. Sodium and potassium concentrations were determined by the routine Clinical Biochemistry laboratory potentiometrically in plasma dilutions using a Beckmann Astra 8 analyser and Na and K ion-selective electrodes. Measured concentrations (mmol Na/l plasma dilution) were multiplied by the ratio ml plasma dilution/ml undiluted plasma to obtain the reported plasma levels, mmol Na/l undiluted plasma—$[\mathrm{Na}]_P$. The sodium reference range established with the instruments in our laboratory had 95 per cent confidence limits of 137–145 mmol/l plasma, and hyponatraemia was considered as $[\mathrm{Na}]_P < 137$ mmol/l.

The change between $[\mathrm{Na}]_P$ on admission and on the first postoperative day was calculated and was termed $\Delta[\mathrm{Na}]$. Similarly, the change between $[\mathrm{K}]_P$ on admission and on the first postoperative day was calculated and was termed $\Delta[\mathrm{K}]$.

The volume of 5 per cent dextrose or 4 per cent dextrose/0·18 per cent saline given intravenously (IV) between admission and the first postoperative blood sample was noted. (These fluids are rendered hypo-osmolar on metabolic consumption of dextrose and will be referred to subsequently as 'hypo-osmolar'.) No attempt was made to standardize or influence the peroperative or postoperative IV fluid regimens.

Patients underwent a wide range of general surgical operations, both elective and emergency. Operations were divided into three groups depending upon their severity: minor (breast biopsy, perianal procedures, varicose veins, etc.); moderate (mastectomy, appendicectomy, sympathectomy, etc.) and major (gastroduodenal surgery, cholecystectomy, colectomy, amputation, vascular reconstruction, etc.). No patients in this series underwent endoscopic urological surgery. Data were expressed as mean ± standard error (s.e.m.) and statistical analysis was by paired and unpaired t tests as appropriate.

Results

Five hundred and fifteen patients were studied; the distribution within subgroups is shown in *Table 1*.

$[Na]_P$ on admission, $[Na]_P^{in}$

The means of $[\mathrm{Na}]_P^{\mathrm{in}}$ in the three operative severity groups were: minor 141·12 ± 0·14 mmol/l; moderate 140·57 ± 0·18 mmol/l; major 139·25 ± 0·30 mmol/l (minor *versus* moderate, $P < 0{\cdot}05$; minor *versus* major, $P < 0{\cdot}001$; moderate *versus* major, $P < 0{\cdot}001$). Seven per cent of patients were hyponatraemic on admission, the distribution within subgroups being shown in *Table 2*.

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Table 1 *Distribution of patients*

Group	Total	$[\text{Na}]^{\text{in}}_{\text{P}}$ recorded	Δ[Na] calculable
Minor	203	180	89
Moderate	167	156	92
Major	145	141	128
Overall	515	477	309

Table 2 *The incidence of hyponatraemia ($[Na]_P<137$ mmol/l) on admission and after surgery*

Group	Pre-operative	Postoperative
Minor	0/180 (0%)	7/89 (7·9%)
Moderate	4/156 (2·6%)	18/92 (19·6%)
Major	29/141 (20·6%)	60/128 (46·9%)
Overall	33/477 (6·9%)	85/309 (27·5%)

Change in $[Na]_P$ after operation, Δ[Na]

By the first postoperative day 27·5 per cent of patients were hyponatraemic, the distribution within subgroups being shown in *Table 2*. The relationship between operative severity and Δ[Na] is shown in *Figure 1*, with a highly significant fall ($P<0{\cdot}001$) in $[\text{Na}]_\text{P}$ occurring in all three groups. Of the 33 patients who were hyponatraemic on admission, 29 subsequently underwent a major operation, with Δ[Na] calculable in 25. Δ[Na] in these patients was −1·40±0·59 mmol/l as compared with −3·68±0·26 mmol/l in the remainder of the major surgery group who were normonatraemic on admission. These changes are significantly different, $P<0{\cdot}001$. When Δ[Na] is plotted against $[\text{Na}]^{\text{in}}_{\text{P}}$, *Figure 2*, a linear relationship is seen, $r=-0{\cdot}45$, $P<0{\cdot}001$.

Elective and emergency surgery

Of the 128 patients undergoing major surgery in whom Δ[Na] was calculable, 92 underwent elective and 36 required urgent or emergency surgery (15 gastrointestinal or colonic operations, 7 ruptured aneurysms, 5 cholecystectomies, 5 laparotomies for trauma, 2 division of adhesions, 1 limb salvage and 1 amputation). The mean $[\text{Na}]^{\text{in}}_{\text{P}}$ of the elective group was not significantly higher than that of the emergency group (139·65±0·34 mmol/l *versus* 138·42±0·69 mmol/l, $P<0{\cdot}1$). Those undergoing emergency gastrointestinal or colonic surgery had a significantly lower $[\text{Na}]^{\text{in}}_{\text{P}}$ than those ($n=13$) undergoing similar elective surgical procedures (135·87±1·20 mmol/l *versus* 139·38±0·68 mmol/l, $P<0{\cdot}05$) and a lesser postoperative fall (−1·73±0·69 mmol/l) *versus* −3·38±0·84 mmol/l. The latter difference was not significant, $P>0{\cdot}1$.

Intravenous fluid administration

The relationship between the volume of hypo-osmolar IV fluid administered (between admission and first postoperative $[\text{Na}]_\text{P}$ measurement) and Δ[Na] is shown in *Figure 3*. Although there is a constant relationship between the volume of IV fluid infused and Δ[Na], a highly significant fall occurs in $[\text{Na}]_\text{P}$ even when no hypo-osmolar fluids are given ($P<0{\cdot}001$). A similar pattern is seen when operative severity is also taken into account, *Figure 4*: significant falls occurred in all groups except minor 0·5 litres ($n=8$, $t=1{\cdot}79$), moderate >1·5 litres ($n=3$) and major no fluid group ($n=12$, $t=1{\cdot}59$).

Change in $[K]_P$ after operation, Δ[K]

$[\text{K}]_\text{P}$ fell after operation, the extent of the fall being inversely related to the severity of operation: minor −0·22±0·04 mmol/l, moderate −0·21±0·05 mmol/l, major −0·08±0·05 mmol/l (minor *versus* major $P<0{\cdot}05$, other comparisons not significant). A consistent relationship between Δ[K] and the volume of hypo-osmolar fluid administered did not exist (no IV fluid, Δ[K] 0·17±0·14 mmol/l; 0·5 litres, Δ[K] −0·09±0·09 mmol/l; 1·0 litres, Δ[K] −0·13±0·08 mmol/l; 1·5 litres, Δ[K] 0·08±0·11 mmol/l; >1·5 litres, Δ[K] −0·30±0·17 mmol/l). There was no relationship between Δ[Na] and Δ[K], $r=0{\cdot}05$.

Clinical outcome

None of the patients who were hyponatraemic on admission or later became so showed obvious neurological sequelae. Seventeen patients died during or after surgery, mortality 3·6 per cent. These patients were admitted with ruptured abdominal aortic aneurysm (eight cases), severe limb ischaemia (four cases), obstructive jaundice (two cases), rectal carcinoma, gastrointestinal haemorrhage and gluteal abscess (one case each). Sixteen of these deaths occurred during or after major surgery. The admission $[\text{Na}]_\text{P}$ of these patients was significantly lower than the remainder of the major surgery group (136·08±1·03 mmol/l *versus* 139·57±0·30 mmol/l, $P<0{\cdot}001$). The initial postoperative change in $[\text{Na}]_\text{P}$, Δ[Na], was no different.

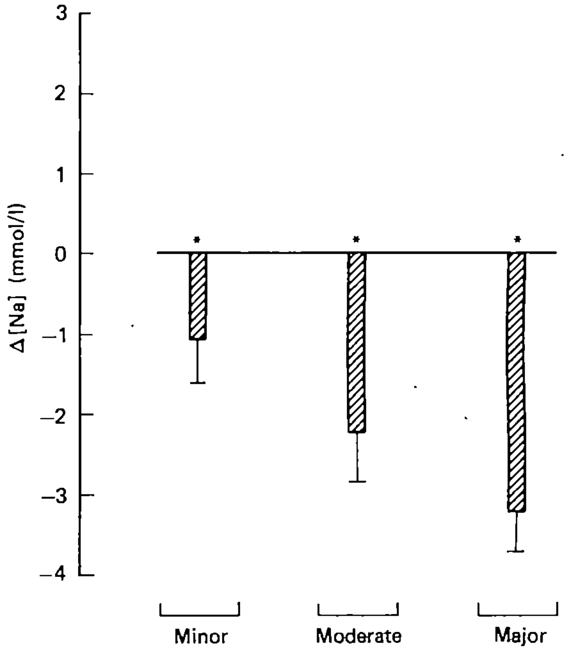

Figure 1 *Relationship between operative severity and Δ[Na]. Histograms show mean values and 2 s.e.m.* * $P<0{\cdot}001$. *Minor* versus *moderate*, $P<0{\cdot}01$: *minor* versus *major*, $P<0{\cdot}001$; *moderate* versus *major*, $P<0{\cdot}02$

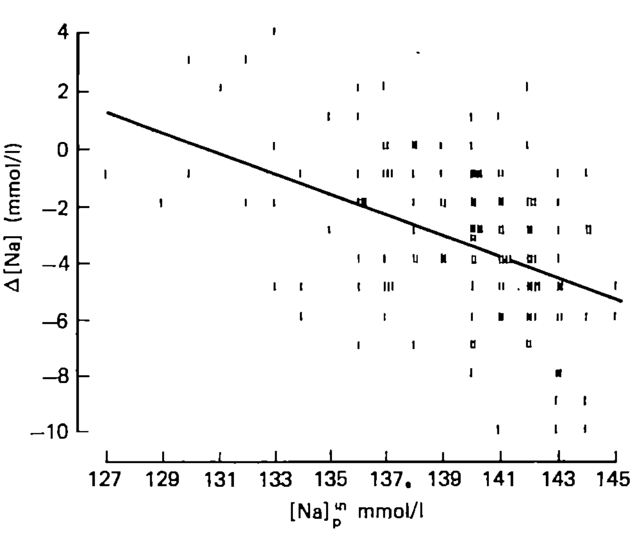

Figure 2 *Relationship between $[Na]_P$ on admission ($[Na]^{in}_P$) and Δ[Na] for patients undergoing major surgery.* $r=-0{\cdot}4541$

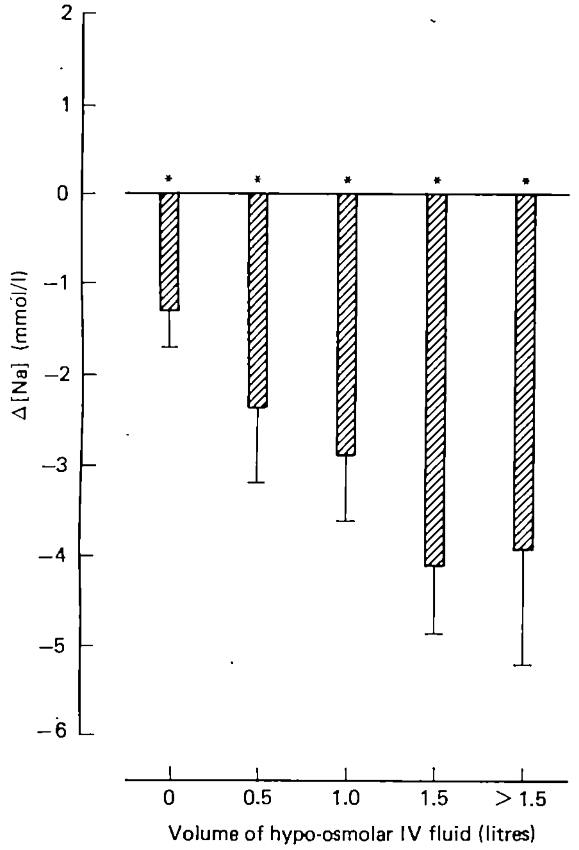

Figure 3 *Relationship between the volume of hypo-osmolar fluid administered before the first postoperative blood sample and* $\Delta[Na]$. *Histograms show mean values and 2 s.e.m.* * $P<0{\cdot}001$

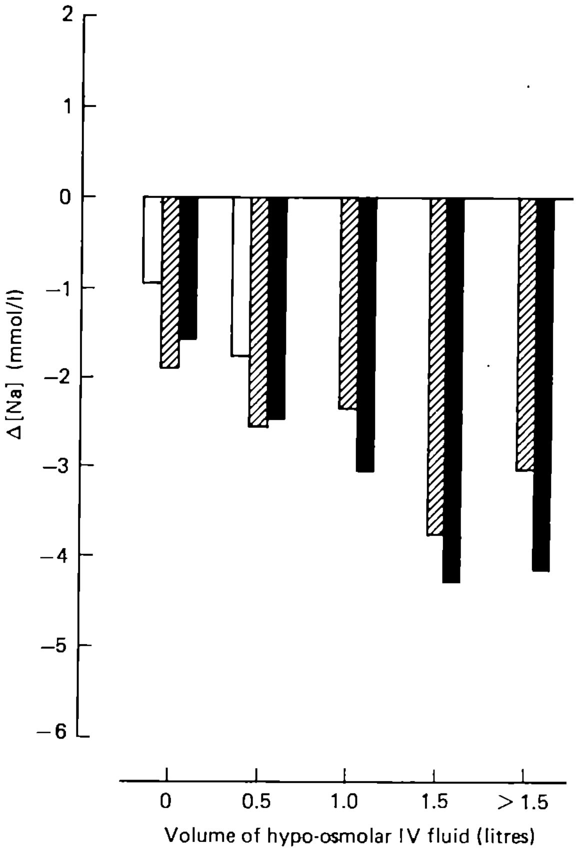

Figure 4 *Relationship between the volume of hypo-osmolar fluid administered (in operative severity groups) and mean* $\Delta[Na]$. □, *Minor;* ▨, *moderate;* ■, *major*

Discussion

In this study, data on pre-operative and postoperative $[Na]_P$ and $[K]_P$ with derived $\Delta[Na]$ and $\Delta[K]$ are to some extent incomplete. Thirty-eight patients (7·4 per cent of the total) did not have $[Na]_P$ measured or recorded on admission to hospital, and in only 309 (60·0 per cent of the total) could the $\Delta[Na]$ be calculated, *Table 1*. The majority of those patients whose data on $\Delta[Na]$ are incomplete were young and undergoing more minor surgery. We do not feel that lack of complete data on these patients invalidates our findings or conclusions: in the minor and moderate surgery groups there was no difference between groups of patients 'with and without $\Delta[Na]$' in terms of age, operation undergone or $[Na]_P$ on admission.

The significant differences in $[Na]_P$ on admission that exist between the three groups of operative severity reflect, to a large extent, the disease processes for which operation is required. Patients presenting for emergency gastrointestinal or colonic surgery have a lower $[Na]_P$ than those presenting for similar elective surgery. Hyponatraemia commonly occurs in many chronic disease states (heart failure, renal failure, neoplasia, etc.) and is often noted when patients present for operation. Of the thirty-three patients presenting with hyponatraemia in this study, thirteen had peritonitis, gastrointestinal perforation or obstruction, eight had severe limb ischaemia or leaking abdominal aortic aneurysm and four had obstructive jaundice. The remaining eight patients had neoplasia or widespread cardiovascular disease in which situations hyponatraemia is not unexpected.

A fall in $[Na]_P$ is well known to occur after injury and major surgery[1,5]. Endogenous antidiuretic hormone release occurs following trauma and operation[11–13] and injudicious administration of hypo-osmolar IV fluid can cause water retention and hyponatraemia. It has been reported that $[Na]_P$ does not change after abdominal surgery when 0·9 per cent saline solution only is given intravenously[14,15], but we found significant falls in $[Na]_P$ even after minor surgery and whether or not hypo-osmolar IV fluids are given. In addition the degree of fall in $[Na]_P$ was related to the volume of hypo-osmolar fluid administered. *Figure 4* suggests an effect of increasing operative severity upon $\Delta[Na]$ within each IV fluid group, although the numbers in several subgroups are too small for adequate comparison. For those patients receiving no hypo-osmolar fluid $\Delta[Na]$ is, as one would expect, significantly greater following moderate ($n=46$) rather than minor ($n=77$) surgery ($-1{\cdot}89\pm0{\cdot}33$ mmol/l *versus* $-0{\cdot}94\pm0{\cdot}28$ mmol/l, $P<0{\cdot}05$). Only 12 patients undergoing major surgery received no hypo-osmolar IV fluid, with $\Delta[Na]$ of $-1{\cdot}58\pm1{\cdot}00$ mmol/l. It has been reported that dilution is commonly insufficient to account for all of the fall observed in $[Na]_P$ as has been shown by consideration of the relationship between $[Osm]_w$ and $[Na]_w$ (mosmol and mmol Na/kg plasma water, respectively) in the postoperative period[1,2]. Osmolal gaps can be seen in patients with a particularly complicated postoperative course[2–7] and have been attributed to isosmotic redistribution of solute caused by an abrupt increase in cell membrane permeability[7,8,10]. In such situations the relationship between $[Osm]_w$ and $[Na]_w$ is both dynamic and changing[7,10]. These relationships were not investigated in the patients considered in this study.

The administration of 0·5 litres of 5 per cent dextrose solution to a patient with a total body water of 40 litres and a $[Na]_P$ of 140 mmol/l would be expected to lower $[Na]_P$ to $\approx 138{\cdot}3$ mmol/l. This is less than the fall seen in those patients receiving 0·5 litres of hypo-osmolar IV fluid postoperatively ($\Delta[Na]=-2{\cdot}36\pm0{\cdot}42$ mmol/l). Of our patients, 135 received no hypo-osmolar IV fluid in the period under consideration, yet their $[Na]_P$ fell significantly ($\Delta[Na]=-1{\cdot}32\pm0{\cdot}21$ mmol/l): even in the subgroup of 77 of these patients undergoing minor surgery there was a highly significant fall ($\Delta[Na]=-0{\cdot}94\pm0{\cdot}28$ mmol/l). The relative contribution of hormonal and membrane permeability changes to these falls in $[Na]_P$ was not assessed in our patients. The finding of significant falls in $[\text{Na}]_{\text{P}}$ when dilution can be excluded as a cause, after even minor surgery, requires further investigation. It is perhaps pertinent that hyponatraemia is not infrequently found in previously healthy people admitted to hospital between 1 and 22 h after major civilian injuries who have been given fluids neither to drink nor intravenously (C. T. G. Flear, unpublished observations). Whether the immediate fall in $[\text{Na}]_{\text{P}}$ after operation is provoked by anaesthesia or operative manipulation of tissues is debatable. It has been previously noted that biopsies from unexposed muscle that had been under gentle retraction differed somewhat from biopsies of a region of the same muscle that had not[16].

The finding that patients who were hyponatraemic on admission had a much lesser fall in $[\text{Na}]_{\text{P}}$ postoperatively than those who were normonatraemic on admission suggests an inverse relationship between $[\text{Na}]_{\text{P}}^{\text{in}}$ and $\Delta[\text{Na}]$. This was seen (*Figure 2*), but with much residual scatter about the relationship. It seems likely that $[\text{Na}]_{\text{P}}$ has already been reduced in hyponatraemic patients by the 'clinical stresses' associated with the illness necessitating surgery. The finding that the admission $[\text{Na}]_{\text{P}}$ of those patients who subsequently died was significantly lower than that of survivors is not unexpected as both $[\text{Na}]_{\text{P}}$ and death reflect the severity of the underlying disease.

Rises in $[\text{K}]_{\text{P}}$ have been described as $[\text{Na}]_{\text{P}}$ falls in patients undergoing upper abdominal surgery[17] and mitral valvuloplasty[18]. Although we saw such shifts on occasions, overall such a relationship was not seen as is shown by consideration of the plot of $\Delta[\text{Na}]$ against $\Delta[\text{K}]$.

As this study was conducted using data from routine blood sampling only, we could not systematically study the course of $[\text{Na}]_{\text{P}}$ in the later part of the postoperative period. A controlled prospective study should be undertaken based on information obtained from our observations to study changes in $[\text{Na}]_{\text{P}}$, $[\text{Na}]_{\text{w}}$ and $[\text{Osm}]_{\text{w}}$ throughout the postoperative period. Particular emphasis needs to be paid to comparing those patients undergoing similar surgery who are normonatraemic and those who are hyponatraemic on admission, as well as to those undergoing minor surgery. It is our view that $[\text{Na}]_{\text{P}}$ may be a useful indicator of clinical well-being in the postoperative surgical patient, and that persistent or unexpected hyponatraemia is more likely to represent emergent or continuing sepsis, tissue ischaemia or other postoperative complication than a primary disturbance of sodium balance; attention should be directed to correcting the underlying disorder, not hyponatraemia.

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References

1. Flear CTG, Bhattacharya SS, Singh CM. Solute and water exchanges between cells and extracellular fluids in health and disturbances after trauma. *J Parent Enter Nutr* 1980; **4**: 98–119.
2. Singh CM. Cellular factors causing disturbances of water and electrolyte metabolism in clinical situations. PhD Thesis, 1971, University of Newcastle upon Tyne.
3. Singh CM, Flear CTG. Why does the plasma sodium level fall after surgery? *Br J Surg* 1968; **55**: 858.
4. Tindall SF, Clark RG. Hyponatraemia in surgical practice. *Br J Surg* 1976; **63**: 150.
5. Chan S, Radcliffe A, Johnson A. The serum sodium concentration after surgical operation: precision permits predictions. *Br J Surg* 1980; **67**: 711–4.
6. Flear CTG. Electrolyte and body water changes after trauma. *J Clin Pathol* 1970; **23** (Suppl 4): 16–31.
7. Flear CTG, Singh CM. The sick cell concept and hyponatraemia. In: Bain WH, Taylor K, ed. *Handbook of Intensive Care*. Bristol: John Wright, 1983: 165–95.
8. Flear CTG, Singh CM. Hyponatraemia and sick cells. *Br J Anaesth* 1973; **45**: 976–94.
9. Flear CTG, Hilton P. Hyponatraemia and severity and outcome of myocardial infarction. *Br Med J* 1979; **1**: 1242–6.
10. Flear CTG, Singh CM. The sick cell concept and hyponatraemia in congestive heart failure and liver disease. *Lancet* 1982; **ii**: 101–2.
11. Shirani KZ, Vaughan GM, Robertson GL *et al*. Inappropriate vasopressin secretion (SIADH) in burned patients. *J Trauma* 1983; **23**: 217–24.
12. Burrows FA, Shutack JG, Crone RK. Inappropriate secretion of antidiuretic hormone in a postsurgical pediatric population. *Crit Care Med* 1983; **11**: 527–31.
13. Chung HM, Kluge R, Schrier RW, Anderson RJ. Postoperative hyponatremia. A prospective study. *Arch Intern Med* 1986; **146**: 333–6.
14. Thomas TH, Morgan DB. Post-surgical hyponatraemia: the role of intravenous fluids and arginine vasopressin. *Br J Surg* 1979; **66**: 540–2.
15. Tindall SF, Clark RG. The influence of high and low sodium intakes on post-operative antidiuresis. *Br J Surg* 1981; **68**: 639–44.
16. Flear CTG, Pickering J, McNeill IF. Observations on water and electrolyte changes in skeletal muscle during major surgery. *J Surg Res* 1969; **9**: 369–82.
17. Dudley HF, Boling EA, Le Quesne LP, Moore FD. Studies on antidiuresis in surgery: effects of anesthesia, surgery and posterior pituitary antidiuretic hormone on water metabolism in man. *Ann Surg* 1954; **140**: 354–67.
18. Wilson GM, Edelman IS, Brooks L, Myrden JA, Harken DE, Moore FD. Metabolic changes associated with mitral valvuloplasty. *Circulation* 1954; **9**: 199–219.

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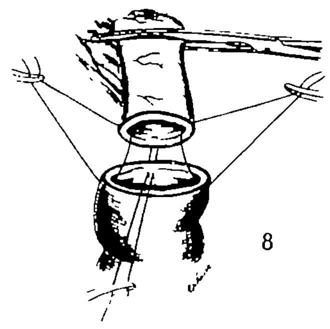
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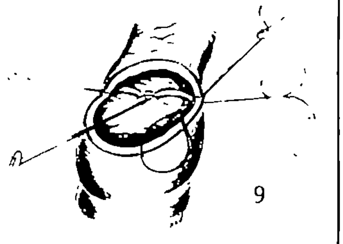
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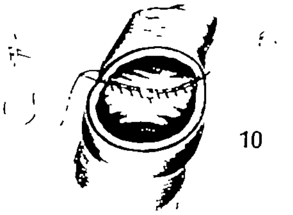
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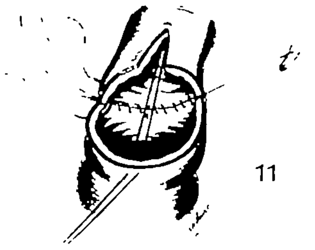
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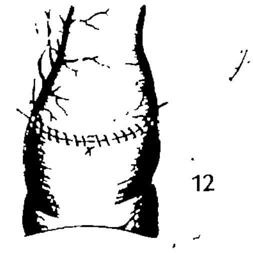
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Insulin resistance in patients with colorectal cancer

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The euglycaemic glucose clamp technique has been used to assess insulin resistance in patients with colorectal adenocarcinoma. Ten cancer patients were studied and compared with control subjects matched for age, sex and nutritional status. Forty-one euglycaemic clamps were performed at one of five different insulin infusion rates (20, 30, 40, 100 or 200 milliunits min^{-1} m^{-2}*). Glucose disposal was significantly decreased in the cancer group at all insulin infusion rates, whilst attained insulin levels and metabolic clearance rates of insulin were comparable in the control and cancer groups. Analysis of dose–response data allowed assessment of sensitivity (insulin concentration of half maximal glucose disposal) and responsiveness (maximal glucose disposal). Responsiveness was significantly reduced in the cancer group (40·3* versus *71·5 μmol* kg^{-1} min^{-1}*;* $P<0{\cdot}001$*), whilst sensitivity was similar (93·7 milliunits* l^{-1} *in controls* versus *90·8 milliunits* l^{-1} *in cancer patients), suggesting a postreceptor defect in insulin action in the cancer group.*

Keywords: Insulin, glucose, colorectal cancer

Patients with cancer often demonstrate abnormalities in glucose metabolism[1,2]. Many previous reports have studied patients with progressive weight loss or advanced disease states and this has led some authorities to suggest that changes in glucose metabolism are the result of malnutrition rather than a cancer effect[3]. However recent reports of patients with limb sarcoma[4], oesophageal carcinoma[5] and non-oat cell lung cancer[6] suggest that abnormalities in glucose metabolism can be detected in the absence of cachexia and without extensive metastatic spread. It has recently been demonstrated, using the hyperglycaemic glucose clamp technique, that non-cachectic patients with gastrointestinal adenocarcinoma show abnormal glucose disposal in the presence of a normal insulin response[7]. This would suggest that insulin resistance is an important factor in the development of abnormal glucose metabolism, and indeed, *in vitro*, skeletal muscle studies in cancer patients would support this hypothesis[2].

In an attempt to quantify, *in vivo*, the effect of insulin resistance on glucose metabolism in patients with gastrointestinal adenocarcinoma, the euglycaemic insulin clamp technique was utilized[8]. By infusing insulin at varying rates, whilst maintaining euglycaemia, dose–response curves may be constructed defining the relationship between glucose disposal and plasma insulin concentration[9].

Patients and methods

Twenty subjects have been studied: a control group of ten subjects and a cancer group of ten patients with colorectal adenocarcinoma. Patients and controls were matched for age, sex and nutritional status. Each group consisted of six men and four women; the mean age of the control group was 68·6 years (range 56–76) and that of the cancer group was 68·5 years (range 54–76). All subjects were within 10 per cent of their ideal body weight (Metropolitan Life Insurance Company tables) and consumed diets containing at least 200 g carbohydrate per day for at least 3 days before the study.

No subject had a family history of diabetes mellitus or was taking drugs known to affect glucose metabolism. All patients were haemodynamically stable and had normal electrolytes, liver function tests and urinary output at the time of study. None were infected, as determined by clinical symptoms and signs, body temperature and leucocyte count. No patient had undergone any surgical procedure in the preceding month.

All studies were commenced at 08·00 h after an overnight fast. An indwelling catheter was sited in an antecubital vein for the infusion of 20 per cent dextrose and insulin. An additional catheter was placed in a dorsal hand vein in order to obtain arterialized venous samples using the heated hand technique[10]. The insulin infusate was prepared in isotonic saline to which 2 ml of the subject's blood per 50 ml of infusate was added, in order to prevent insulin adsorption to plastic surfaces. Each study was commenced after a 45 min rest period. The plasma insulin level was acutely elevated by a 10 min priming insulin infusion[8], followed by a 110 min constant insulin infusion at rates of either 20, 30, 40, 100 or 200 milliunits min^{-1} m^{-2}. Hypoglycaemia was avoided by the infusion of 20 per cent dextrose from 4 min onwards. Rates of dextrose infusion were empirically set, depending on the subject's body weight, from 4–10 min. Thereafter the plasma glucose was estimated every 5 min and these values utilized employing a negative feedback algorithm[8] to compute the dextrose infusion rate necessary to maintain steady state euglycaemia.

Twenty-one euglycaemia clamp procedures were performed in the control group; four at constant rate infusions of insulin of 20 milliunits min^{-1} m^{-2}, five at 30 milliunits min^{-1} m^{-2}, five at 40 milliunits min^{-1} m^{-2}, three at 100 milliunits min^{-1} m^{-2}, and four at 200 milliunits min^{-1} m^{-2}. Nine control subjects had two such studies at different rates and one had three studies performed. Each cancer patient had two studies at different insulin infusion rates; three at 20 milliunits min^{-1} m^{-2}, five at 30 milliunits min^{-1} m^{-2}, five at 40 milliunits min^{-1} m^{-2}, three at 100 milliunits min^{-1} m^{-2} and four at 200 milliunits min^{-1} m^{-2}. At least 1 week was allowed between repeated investigations.

Blood samples were obtained at 20 min intervals for determination of plasma insulin.

Plasma glucose was measured by a glucose oxidase method (Yellow Springs Instruments Co. Inc.). Plasma insulin was determined by radioimmunoassay using a commercial kit (Amersham).

The rate of glucose infusion was calculated for each 20 min period, from 20 to 120 min, throughout all procedures. The mean of these values, during steady state conditions, equals the rate of glucose disposal (M, μmol kg^{-1} min^{-1}). As none of the subjects exhibited glycosuria during these studies, no urinary correction was necessary. The steady state insulin concentration was calculated as the mean of the insulin concentrations from 20 to 120 min. The Lineweaver-Burk transformation (double reciprocal plot of glucose disposal and mean insulin concentration) was used to analyse the dose–response curves from these data.

As the rate of insulin infusion was constant, the metabolic clearance rate of plasma insulin (MCR, litres min^{-1} m^{-2}) was calculated as follows:

$$\mathrm{MCR}=\frac{\text{Insulin infusion rate}}{\text{Increase in plasma insulin above basal}}$$

The insulin concentration of the infusion fluid was estimated from infusate samples taken at the end of the infusion period.

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Statistical analysis

Results are expressed as the mean ± s.e.m., except where indicated. Statistical significance has been assessed using Student's t test. Linear regression was calculated by the method of least squares and differences between curves were assessed using covariant analysis.

Results

Patient details of the cancer group are illustrated in *Table 1*. There was no significant difference in nutritional indices between the two groups (*Table 2*).

Baseline glucose levels were elevated in the cancer group ($5{\cdot}3 \pm 0{\cdot}2$ *versus* $4{\cdot}4 \pm 0{\cdot}1$ mmol l^{-1}; $P<0{\cdot}05$), but there was no significant difference in basal insulin levels between the two groups (9 ± 1 milliunits l^{-1} in controls *versus* 10 ± 1 milliunits l^{-1} in cancer patients). In both groups plasma glucose was well maintained at basal levels throughout the period of insulin infusion; the coefficient of variation of plasma glucose concentration during the study period, when compared with basal levels, was $6{\cdot}9 \pm 0{\cdot}8$ per cent for controls and $4{\cdot}9 \pm 0{\cdot}5$ per cent for the cancer group (*Figure 1*).

In both the control and cancer groups insulin levels increased with the dose of insulin infused, there being no significant difference in achieved insulin concentration between the two groups (*Table 3*). The MCR tended to decrease at higher infusion rates, but there was no significant difference between the two groups (*Table 4*). The mean MCR for all studies was $0{\cdot}58 \pm 0{\cdot}04$ litres min^{-1} m^{-2} in controls and $0{\cdot}57 \pm 0{\cdot}04$ litres min^{-1} m^{-2} in the cancer group.

Glucose disposal was significantly decreased at all insulin infusion rates in the cancer group (*Table 5*), when compared with control subjects. Increasing plasma insulin concentration resulted in a glucose disposal response which approached a maximum (*Figure 2*), and Lineweaver-Burk transformation of the data demonstrated a significant linear relationship between the variables in both groups ($P<0{\cdot}001$). In the cancer group maximal glucose disposal was 40·3 μmol kg^{-1} min^{-1} (95 per cent confidence limits 31·2–56·8), as compared with 71·5 μmol kg^{-1} min^{-1} (95 per cent confidence limits 59·9–88·5) in controls ($P<0{\cdot}001$). Glucose disposal appeared to be unaffected by the tumour class.

Table 1 *Patient details in the cancer group*

Patient no.	Age (years)	Sex	Primary site	Dukes' classification	Clamps (milliunits min^{-1} m^{-2})
1	66	F	Caecum	C_1	20, 100
2	72	F	Sigmoid	C_1	20, 40
3	73	F	Sigmoid	B_2	30, 40
4	76	M	Transverse	C_2	30, 200
5	54	M	Sigmoid	B_2	20, 40
6	72	M	Caecum	C_2	30, 200
7	67	M	Rectum	'D'	30, 200
8	66	F	Ascending	C_1	40, 100
9	70	M	Sigmoid	'D'	100, 200
10	69	M	Rectum	'D'	30, 40

Table 2 *Nutritional indices*

	Controls	Cancer group
Weight (kg)	70±2	68±2
Weight loss (%)	3±1	3±1
Percentage of ideal weight	100±1	99±1
Triceps skinfold (mm)		
Men	9±0·4	9±0·4
Women	15±0·8	15±0·7
Midarm muscle circumference (mm)		
Men	242±2	247±3
Women	195±2	196±2
Haemoglobin (g dl^{-1})	13·4±0·2	13·2±0·3
Lymphocyte count (10^{-9} cells l^{-1})	1·68±0·06	1·68±0·06
Albumin (g l^{-1})	39±1	39±1

All values shown are the mean ± s.e.m.

In contrast, the plasma concentration of insulin required to achieve a half maximal glucose disposal response was comparable in both groups ($93{\cdot}7 \pm 11{\cdot}7$ milliunits l^{-1} in controls, $90{\cdot}8 \pm 18{\cdot}4$ milliunits l^{-1} in cancer patients; 95 per cent confidence limits).

Discussion

Glucose metabolism is recognized to be abnormal in the cancer bearing state[1,2,11,12] and there is some evidence to suggest that this may, in part, be related to the presence of insulin resistance[2,7]. Whilst *in vitro* studies on skeletal muscle from cancer patients have demonstrated reduced glycogen synthesis and glycolysis, in response to insulin, it has proved difficult to investigate insulin resistance, both quantitatively and qualitatively, *in vivo*[13,14]. However, utilizing the multiple dose euglycaemic clamp technique[9,15] allows these parameters to be assessed. Whilst dose–response curves should ideally be constructed by performing euglycaemic clamps at all insulin doses in the same subject, this was not possible in the present study as this would have necessitated deferring surgery.

Insulin resistance may be defined as a state in which normal concentrations of insulin elicit less than normal responses. Kahn[16] has suggested that insulin resistance may be subdivided into two general categories, decreased insulin sensitivity and decreased insulin responsiveness. In the former (prereceptor defect) the dose–response curve is shifted to the right and increased concentrations of insulin may overcome this deficit to achieve a normal maximal response. Decreased insulin responsiveness cannot be overcome by administering supraphysiological quantities of insulin and as there is usually a surplus of insulin receptors on the cell membrane, this is considered to be related to alterations in intracellular metabolism (postreceptor defect).

In the present study the euglycaemic clamp technique was utilized to examine the dose–response relationship between plasma insulin concentration and glucose disposal in patients with colorectal cancer. Sigmoid dose–response curves were obtained in both groups (*Figure 2*), there being a significant difference between the two groups ($P<0{\cdot}001$). A sigmoid dose–response curve is the expected response to variable dose insulin infusion[15].

Sensitivity may be assessed by the insulin concentration necessary to achieve half maximal glucose disposal (K_m)[17]. This was 93·7 milliunits l^{-1} in control subjects and 90·8 milliunits l^{-1} in the cancer group. These values, however, are calculated from the total glucose uptake and represent both insulin mediated and non-insulin mediated glucose disposal. Bergman *et al.*[17] have demonstrated that in the physiological range of insulin concentration (<100 milliunits l^{-1}), there exists a linear relationship between glucose disposal and insulin concentration (that portion of the sigmoid dose–response curve which approaches a linear relationship), and that extrapolation of this curve to zero insulin produces an estimate of insulin-independent glucose disposal. These estimates of insulin-independent glucose disposal (*Figure 3*) can be used to correct the logarithmic insulin dose–response curve by subtracting these values from glucose disposal at each insulin level. The K_m for controls then increases to 118·7 milliunits l^{-1} and that of the cancer group becomes 119·8 milliunits l^{-1}. These results are similar to results for corrected K_m reported in the literature in normal subjects[17].

In contrast there was a marked difference in responsiveness as assessed by the maximal glucose disposal rate (V_{max})[17]. Although we have not conclusively demonstrated that the dose–response curve of the control group approaches a plateau, the estimated value of V_{max} in our control group, 71·5 μmol kg^{-1} min^{-1}, is comparable to values reported by other authors in elderly subjects[17]. Cancer patients showed a significantly reduced maximal glucose disposal rate of 40·3 μmol kg^{-1} min^{-1}

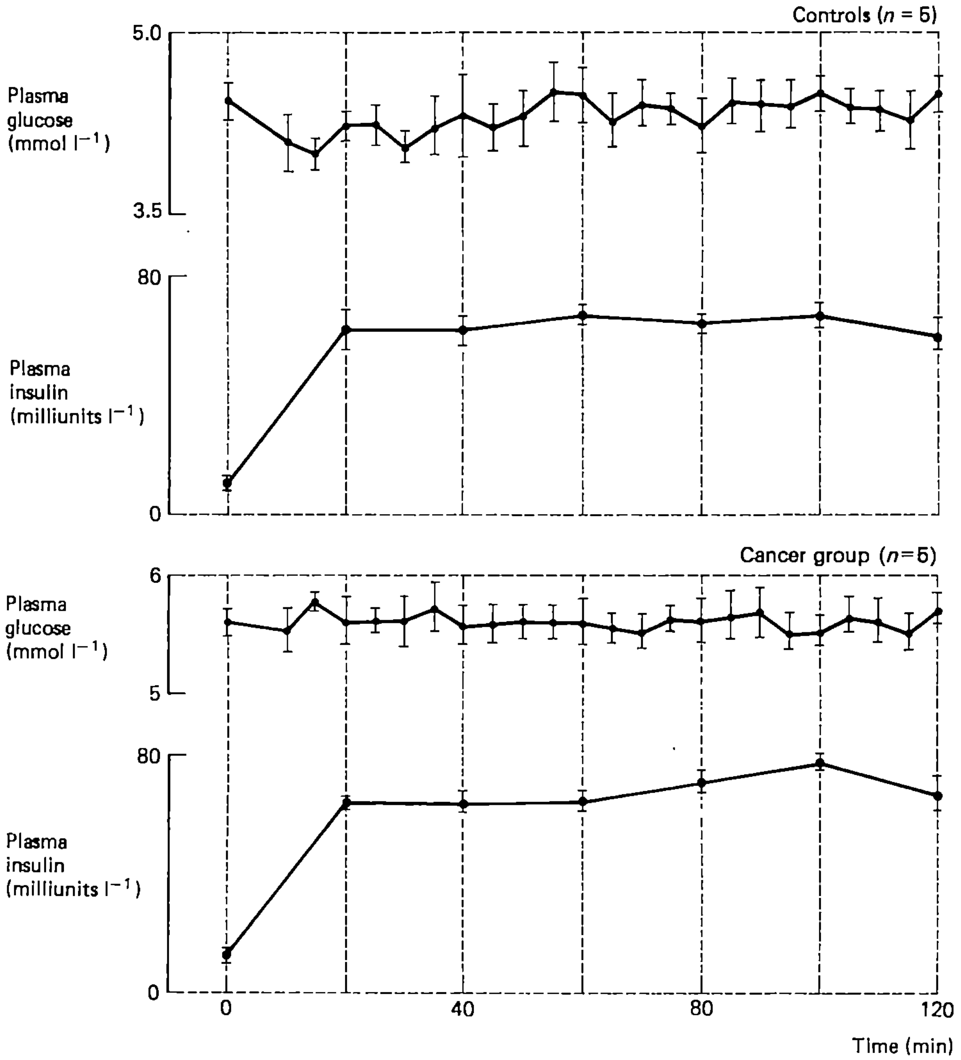

Figure 1 *Glucose and insulin concentrations during euglycaemic clamp procedures at a constant rate insulin infusion of 30 milliunits min^{-1} m^{-2} to illustrate the control of glucose and insulin levels. Glucose levels were 'clamped' at each subject's baseline glucose level. Points shown indicate the mean ± s.e.m.*

Table 3 *Achieved insulin concentrations during euglycaemic clamp procedures*

	Controls		Cancer group		
Insulin infusion rate (milliunits min^{-1} m^{-2})	n	Insulin concentration (milliunits l^{-1})	n	Insulin concentration (milliunits l^{-1})	P
20	4	36±2	3	33±2	n.s.
30	5	65±2	5	69±1	n.s.
40	5	67±4	5	67±3	n.s.
100	3	226±18	3	207±10	n.s.
200	4	688±201	4	614±187	n.s.

The apparent small change in achieved insulin concentrations between the clamps performed at 30 and 40 milliunits min^{-1} m^{-2} are related to variations in basal insulin levels, metabolic clearance of insulin and the determined insulin infusion rate. n.s., not significant

($P < 0{\cdot}001$). These values are based on the amount of exogenous glucose infused and do not include endogenous glucose production. Whilst Holroyde *et al.*[18] have shown that, in response to parenteral nutrition, endogenous glucose production in cancer patients is reduced to the same degree as in controls, there is also evidence to suggest that excessive glucose–lactate recycling may not be suppressed by glucose infusion in cancer patients[12]. Whilst this may be the case in cancer subjects with progressive weight loss[1], where glucose–lactate recycling

Table 4 *Metabolic clearance rate of insulin during euglycaemic clamp procedures*

	Controls		Cancer group		
Insulin infusion rate (milliunits min^{-1} m^{-2})	n	MCR (l min^{-1} m^{-2})	n	MCR (l min^{-1} m^{-2})	P
20	4	0·78±0·06	3	0·84±0·03	n.s.
30	5	0·55±0·03	5	0·51±0·02	n.s.
40	5	0·72±0·04	5	0·66±0·02	n.s.
100	3	0·42±0·04	3	0·47±0·02	n.s.
200	4	0·36±0·08	4	0·40±0·07	n.s.

n.s., not significant. MCR, metabolic clearance rate

Table 5 *Rates of glucose disposal, M, during euglycaemic clamp procedures*

	Controls		Cancer group		
Insulin infusion rate (milliunits min^{-1} m^{-2})	n	M (μmol kg^{-1} min^{-1})	n	M (μmol kg^{-1} min^{-1})	P
20	4	19·1±1·1	3	11·9±0·7	<0·005
30	5	30·0±2·0	5	15·4±0·9	<0·001
40	5	32·6±2·2	5	16·8±1·4	<0·001
100	3	48·1±3·2	3	33·4±1·2	<0·01
200	4	57·4±2·5	4	38·9±3·1	<0·001

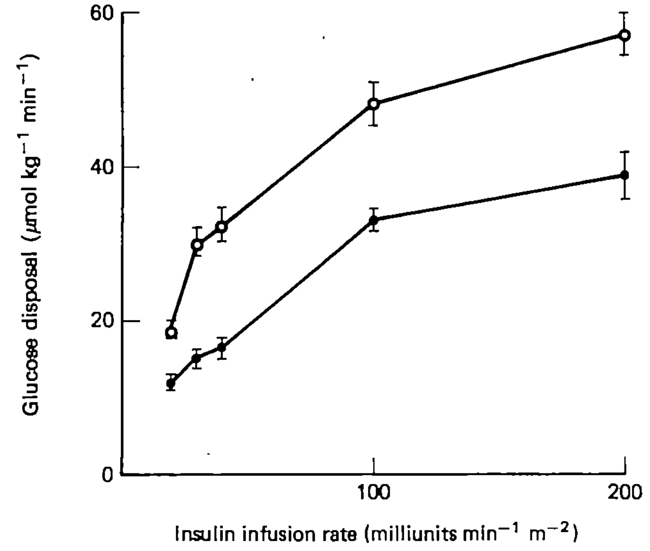

Figure 2 *The effect of colorectal cancer on glucose disposal during euglycaemic clamp procedures at variable insulin infusion rates.* ○, *Controls;* ●, *cancer group. Points shown indicate the mean ± s.e.m.*

may be a significant factor in the development of cachexia, the present patients with colorectal cancer are comparable to those studied by Kokal *et al.*[19], where little evidence of glucose–lactate recycling could be demonstrated. Thus, even if no suppression of endogenous glucose production occurred in the present cancer group, the difference observed between the cancer and control groups would probably still remain significant, although tracer studies would be necessary to confirm this.

These results would suggest that patients with colorectal cancer show impaired responsiveness to insulin in the presence of normal sensitivity to insulin. There is normally a surplus of insulin receptors and, although insulin receptor numbers were not determined in the present study, other authors have shown no difference in insulin receptors in cancer patients[20,21]. Thus a postreceptor defect in insulin action would appear to be the most likely cause of impaired glucose disposal.

The primary effect of insulin is to enhance the uptake of glucose by peripheral tissues, mainly skeletal muscle and fat[22]. Bjorntorp *et al.*[23,24] have shown that <1 per cent of an intravenous glucose load is taken up by adipose tissue. Thus the major effect of insulin is on skeletal muscle and this would represent a probable site of insulin resistance in the patient with colorectal cancer. Studies of the forearm *in vivo*, which are planned, are needed to confirm that skeletal muscle is the major site of insulin resistance.

Could the presence of host insulin resistance be of biological advantage to the tumour itself? Colorectal tumour cells have been shown to possess insulin receptors[25] and these do not demonstrate the usual down-regulation on exposure to insulin seen in normal tissues[26]. The presence of host peripheral insulin resistance may contribute to the depletion of the host, enabling the tumour to act as a 'glucose trap' as suggested by Shapot[27]. In cancer patients with progressive weight loss, increased glucose–lactate recycling and malnutrition itself, by further impairing glucose disposal and reducing insulin release[28], may compound the metabolic abnormality.

The cause of insulin resistance is not clear from the present data. In other disease states, trauma and sepsis, in which a postreceptor defect in insulin action has been demonstrated[29], it has been postulated that the ambient hormonal milieu[30], increased free fatty acid utilization[31] and increased intracellular leucine levels[32,33] may be implicated in the development of impaired glucose utilization. Whilst there is little information with regard to glucagon and adrenaline levels in patients with malignancy, it has been shown that cortisol levels are normal in patients with gastrointestinal malignancy who demonstrate abnormal glucose disposal[7]. Certainly, *in vivo* studies show no significant difference in palmitic acid and leucine utilization by skeletal muscle in the cancer bearing patient.

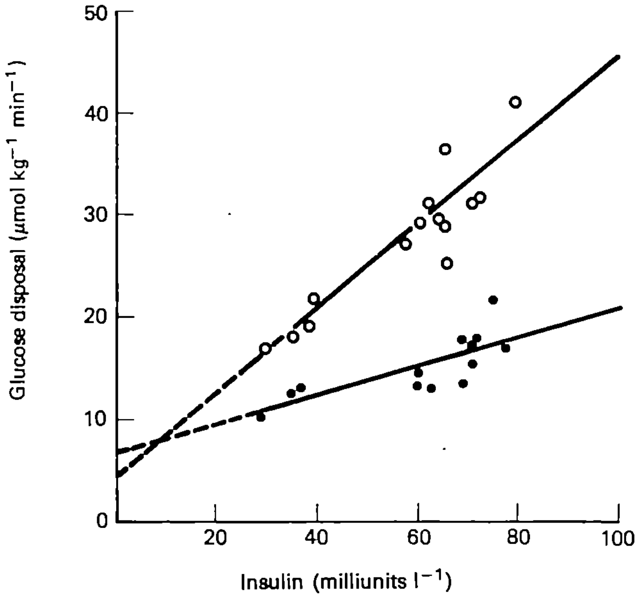

Figure 3 *The relationship of glucose disposal to insulin concentration in the physiological insulin range* (<*100 milliunits* l^{-1}). *Extrapolation to zero insulin yields an estimate of non-insulin dependent glucose disposal.* ○, *Controls:* $y = 0{\cdot}414x + 4{\cdot}06$ $P < 0{\cdot}001$; ●, cancer group: $y = 0{\cdot}141x + 6{\cdot}59$ $P < 0{\cdot}001$

In conclusion, the present study demonstrates that glucose is abnormal in patients with colorectal cancer. This is due to the presence of insulin resistance and may be related to a postreceptor defect in insulin action. Further studies are planned to determine the site of insulin resistance and any effect this may have on skeletal muscle amino acid and fat metabolism.

References

1. Holroyde CP, Reichard GA. Carbohydrate metabolism in cancer cachexia. *Cancer Treat Rep* 1981; **65** (Suppl. 5): 55–9.
2. Lundholm K, Holm G, Schersten T. Insulin resistance in patients with cancer. *Cancer Res* 1978; **38**: 4665–70.
3. Jasani B, Donaldson LJ, Ratcliffe JG, Sokhi GS. Mechanism of impaired glucose tolerance in patients with neoplasia. *Br J Cancer* 1978; **38**: 287–92.
4. Norton JA, Maher M, Wesley R, White D, Brennan MF. Glucose intolerance in sarcoma patients. *Cancer* 1984; **54**: 3022–7.
5. Burt ME, Aoki T, Gorschboth CM, Brennan MF. Peripheral tissue metabolism in cancer-bearing man. *Ann Surg* 1983; **198**: 685–91.
6. Heber D, Chlebowski RT, Ishibashi DE, Herrold JN, Block JB. Abnormalities in glucose and protein metabolism in noncachectic lung cancer patients. *Cancer Res* 1982; **42**: 4815–19.
7. Copeland GP, Al-Sumidaie AM, Leinster SJ, Davis JC, Hipkin LH. Glucose metabolism in patients with gastrointestinal malignancy but without excessive weight loss. *Eur J Surg Oncol* 1987; **13**: 11–16.
8. DeFronzo RA, Tobin JD, Andres R, Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol* 1979; **237**: E214–23.
9. Kolterman OG, Insel LJ, Saekow M, Olefsky JM. Mechanisms of insulin resistance in human obesity. Evidence for receptor and post receptor defects. *J Clin Invest* 1980; **65**: 1272–84.
10. McGuire EAH, Helderman JH, Tobin JD, Andres R, Berman M. Effects of arterial versus venous sampling on analysis of glucose kinetics in man. *J Appl Physiol* 1976; **41**: 565–73.
11. Lundholm K, Edstrom S, Ekman L, Karlberg I, Schersten T. Metabolism in peripheral tissues in cancer patients. *Cancer Treat Rep* 1981; **65** (Suppl. 5): 79–83.

12. Heber D, Byerly LO, Chlebowski RT. Metabolic abnormalities in the cancer patient. *Cancer* 1985; **55**: 225–9.
13. Marks PA, Bishop JS. Glucose metabolism in subjects with neoplastic disease: response to insulin and glucose tolerance. Follow up studies. *Proc Am Assoc Cancer Res* 1957; **2**: 228.
14. Bishop JS, Marks PA. Studies on carbohydrate metabolism in patients with neoplastic disease II. Response to insulin administration. *J Clin Invest* 1959; **38**: 668–72.
15. Rizza RA, Mandarino LJ, Gerich JE. Dose-response characteristics for effects of insulin on production and utilization of glucose in man. *Am J Physiol* 1981; **240**: E630–9.
16. Kahn CR. Insulin resistance, insulin insensitivity and insulin unresponsiveness, a necessary distinction. *Metabolism* 1978; **27**(2): 1893–902.
17. Bergman RN, Finegood DT, Ader M. Assessment of insulin sensitivity *in vivo*. *Endo Rev* 1985; **6**: 45–86.
18. Holroyde CP, Myers RN, Smink RD, Putnam RC, Paul P, Reichard GA. Metabolic response to total parenteral nutrition in cancer patients. *Cancer Res* 1977; **37**: 3109–14.
19. Kokal WA, McCulloch A, Wright PD. Glucose turnover and recycling in colorectal carcinoma. *Ann Surg* 1983; **198**: 601–4.
20. Kisner D, Hamosh M, Blecher M, Haller D, Jacobs E, Petersen B, Schein PS. Malignant cachexia: insulin resistance and insulin receptors. *Proc Am Soc Clin Oncol* 1978; **19**: 796.
21. Schein PS, Kisner D, Haller D, Blecher M, Hamosh M. Cachexia of malignancy. Potential role of insulin in nutritional management. *Cancer* 1979; **43**: 2070–6.
22. DeFronzo RA, Jacot E, Jequier E, Maeder E, Wahren J, Felber JP. The effect of insulin on the disposal of intravenous glucose: results from indirect calorimetry and hepatic and femoral venous catheterization. *Diabetes* 1981; **30**: 1000–7.
23. Bjorntorp P, Berchtold P, Larsson B. The glucose uptake of human adipose tissue in obesity. *Eur J Clin Invest* 1971; **1**: 480–3.
24. Bjorntorp P, Sjostrom L. Carbohydrate storage in man. Speculations on some quantitative considerations. *Metabolism* 1978; **27**(2): 1853–65.
25. Forgue-Lafitte ME, Horvat A, Rosselin G. Insulin binding by a cell line (HT29) derived from human colonic cancer. *Mol Cell Endocrinol* 1979; **14**: 123–30.
26. Wong M, Holdaway IM. Insulin binding by normal and neoplastic colon tissue. *Int J Cancer* 1985; **35**: 335–41.
27. Shapot VS. On the multiform relationships between the tumour and the host. *Adv Cancer Res* 1979; **30**: 89–150.
28. Smith SR, Edgar PJ, Pozefsky T, Chhetri MK, Prout TE. Insulin secretion and glucose tolerance in adults with protein calorie malnutrition. *Metabolism* 1975; **24**: 1073–84.
29. Black PR, Brooks DC, Bessey PQ, Wolfe RR, Wilmore DW. Mechanisms of insulin resistance following injury. *Ann Surg* 1982; **196**: 420–35.
30. Bessey PQ, Watters JM, Aoki TT, Wilmore DW. Combined hormonal infusion simulates the metabolic response to injury. *Ann Surg* 1984; **200**: 264–81.
31. Nordenstrom J, Carpentier YA, Askanazi J *et al.* Free fatty acid mobilization and oxidation during total parenteral nutrition in trauma and infection. *Ann Surg* 1983; **198**: 725–35.
32. Askanazi J, Furst P, Michelsen CB *et al.* Muscle and plasma amino acids after injury: hypocaloric glucose vs amino acid infusion. *Ann Surg* 1980; **191**: 465–72.
33. Abumrad NN, Robinson RP, Gooch BR, Lacy WW. The effect of leucine infusion on substrate flux across the human forearm. *J Surg Res* 1982; **32**: 453–63.

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Use of sodium nitroprusside induced hypotensive anaesthesia for reducing blood loss in patients undergoing lienorenal shunts for portal hypertension

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A randomized study was performed on 18 patients to determine whether hypotensive anaesthesia, induced by sodium nitroprusside (SNP), would reduce blood loss during elective proximal lienorenal shunt operations for portal hypertension which was due to extrahepatic obstruction or non-cirrhotic portal fibrosis. Eight patients received SNP intraoperatively to reduce the systolic blood pressure to below 95 mmHg, and there were 10 control patients. Blood loss, the number of units of blood transfused, and urine output during surgery were measured together with the postoperative drainage from the abdominal and chest tubes over the first 24 h. There was a significantly lower blood loss (mean ± s.d. 517 ± 220 versus *1286 ± 523 ml;* $P<0.01$*) and number of units of blood transfused was less (0·9 ± 0·9* versus *3·0 ± 1·2;* $P<0.01$*) in the SNP patients than in the controls. The urine output was greater in the SNP group (606 ± 211* versus *399 ± 139 ml, n.s.). Postoperative drainages from the chest and abdomen were similar. Hypotensive anaesthesia with SNP reduces operative blood loss and transfusion requirement in patients with good liver function undergoing proximal lienorenal shunts for portal hypertension.*

Keywords: Nitroprusside, portal hypertension surgery, blood loss

Portal hypertension is the most common cause of upper gastrointestinal bleeding in India[1] where it is often due to extrahepatic obstruction and non-cirrhotic portal fibrosis. In both diseases the liver function is well preserved and surgical treatment carries a low operative mortality and few complications. The preferred operation is a splenectomy and a central lienorenal shunt. Although not technically difficult it may be accompanied by considerable bleeding and can thus only be performed in centres where large amounts of blood are available for transfusion. In India such centres are few and patients requiring surgery are many so that a substantial number die during a bleeding episode while awaiting a corrective procedure. A method for reducing this blood loss would be of considerable value. In this study we have investigated the use of sodium nitroprusside (SNP) hypotensive anaesthesia, which has been shown to decrease bleeding during other operations[2–4], in reducing blood loss in patients undergoing elective, proximal, lienorenal shunts for portal hypertension.

Patients and methods

Patients

Twenty patients, 16 males and 4 females, were included in this study. Their ages ranged from 10 to 46 years (mean 20 years). Fifteen patients had extrahepatic obstruction and five had non-cirrhotic portal fibrosis. Patients with cirrhosis and children below the age of 10 were excluded. The patients were randomized into the SNP and control groups using a table of random numbers. The pre-operative investigations and preparation, surgical technique and postoperative management were undertaken by the same surgical and anaesthetic teams and were identical in both groups.

Sodium nitroprusside administration

Fifty milligrams of freeze-dried SNP powder was dissolved in 500 ml 5 per cent dextrose and this solution was infused through a separate line protected from light. The infusion rate in the beginning was six drops per minute and this was later adjusted to bring down the systolic pressure to between 85 and 95 mmHg. The total dose did not exceed 1 mg/kg. Each patient in both SNP and control groups received 20 mg of propranolol orally before surgery to control a compensatory increase in heart rate.

Monitoring

The following parameters were monitored during the operation and postoperatively:

1. Arterial pressure by a radial artery cannula.
2. Central venous pressure: this was used by the anaesthetist as a guide to blood replacement, and maintained to within 3 cm of its initial level.
3. The urine output was measured every hour.
4. Arterial blood gases were estimated in eight SNP and seven control patients to detect, at an early stage, any metabolic acidosis caused by SNP administration.
5. Portal pressure: this was monitored via a pressure transducer and a cannula in the right gastro-epiploic vein. The changes in portal pressure before and after SNP was started and after the completion of the anastomosis were recorded.
6. Units of blood transfused.
7. Blood loss: this was estimated by a method described by Gupta[5]. This consists of first washing the sponges in water, collecting the eluted fluid and adding to this all the fluid removed from the operative field. The total volume (V) and the haemoglobin concentration of this fluid (opHb) were noted. The blood loss was calculated by the formula

$$\text{Operative blood loss} = V \times \text{opHb}/\text{patient's Hb}$$

8. Drainage from the abdominal and chest tubes was measured during the first 24 h postoperatively.
9. The blood haemoglobin concentration, and liver function tests (serum bilirubin, alkaline phosphatase and transaminases) were recorded before and 48 h after surgery.

Statistical methods

The blood loss, number of units transfused, and the urine output in the SNP and control groups were compared using Wilcoxon's rank test for non-parametric data. The correlations between arterial systolic pressure and blood loss and the portal pressure and blood loss were determined by using linear regression analysis.

Results

Of the 20 patients studied, 10 were randomized into the SNP group and 10 into the control group. However two patients in the SNP group were excluded from the study, one because his

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blood pressure did not fall to 95 mmHg after SNP and the other because he developed ventricular ectopic beats.

The patients were fairly well matched for age and weight but, despite randomization, the control group had more males and more patients with extrahepatic obstruction (*Table 1*).

1. Arterial pressure: all the patients included in the test group became hypotensive during SNP administration and their systolic arterial pressures were maintained between 90 and 95 mmHg. In the control patients the systolic pressures ranged from 100 to 150 mmHg and remained so during the operation.

2. Central venous pressure was maintained at its original level with fluctuations of not more than 3 cm saline.

3. Urine output was higher in the SNP cases in which it was 606±211 ml (mean±s.d.) than in the controls 399±138 ml.

4. The arterial blood gases, when measured in eight test cases and seven controls, remained normal throughout the operation.

5. Portal pressures were slightly lower in SNP patients (33·2±3·8 cm saline) than in the controls (36·4±5·9 cm saline). On administration of SNP the portal pressure was seen to fall by 6·0–8·0 cm saline; in the controls the portal pressure remained at its original level. After the lienorenal anastomosis was fashioned the fall of pressure (mean±s.d.) was 6·2±3·2 cm saline in the SNP group and 7·9±4·5 cm in the controls.

6. The blood transfusion requirement to maintain the central venous pressure to within 3 cm of basal levels was significantly less ($P<0\cdot01$) in the SNP group (mean±s.d.=0·9±0·9 units, range 0–3 units per patient) than in the controls (3·0±1·2 units, range 2–6 units per patient). In three SNP patients no blood transfusion was given during the operation (*Table 2*).

7. The calculated blood loss in the SNP group ranged from 215 to 1000 ml (mean±s.d.=517±220 ml). In the controls it ranged from 600 to 2500 ml (1286±523 ml) and was significantly greater ($P<0\cdot01$) (*Table 2*).

The blood loss correlated with the mean operative arterial systolic pressure ($r=0\cdot63$) and with the mean portal pressure before anastomosis ($r=0\cdot44$).

8. The postoperative chest and abdominal drainages were similar in the first 24 h. In the SNP group they averaged 164 and 96 ml respectively and in the controls they were 91 and 122 ml. The differences are not significant.

9. The postoperative haemoglobin levels were 0·33 mmol/l higher than the pre-operative levels in the SNP group, and 0·16 mmol/l higher in the control group. The liver function tests were unaltered except for occasional and transient elevations in serum bilirubin and transaminases in some patients in each group.

Discussion

Our study suggests that hypotensive anaesthesia using SNP can reduce the operative blood loss and transfusion requirement in patients with good liver function who undergo splenectomy and lienorenal shunts for portal hypertension. This operation is especially suited to the majority of patients who have very large spleens and well preserved liver function[1]. The spleen, which is vulnerable to trauma and may be associated with hypersplenism[1], is removed. The large splenic vein results in a low rate of shunt thrombosis and, perhaps because of the good liver function and low protein vegetarian diets of these patients, post-shunt encephalopathy is rare. Hypotensive anaesthesia has been used to reduce bleeding or to facilitate difficult procedures in vascular surgery, neurosurgery, orthopaedics, urology, ophthalmology, otorhinolaryngology, plastic and spinal surgery and in breast surgery[2,3,6]. It has not been used previously in operations for portal hypertension, and our results suggest that it may also be useful in these situations in which the portal venous pressure is abnormally high.

Table 1 *Distribution of cases*

	SNP (8)	Control (10)
Age (years)	23±11	17±10
Weight (kg)	44±7	37±11
Male:female	5:3	9:1
EHO:NCPF*	5:3	8:2

* EHO, extrahepatic obstruction; NCPF, non-cirrhotic portal fibrosis

Table 2 *Blood loss and transfusions required*

	SNP (8)	Control (10)
Blood loss (ml)		
Mean±s.d.	517±220	1286±523
Range	215–1000	600–2500
Transfusions (units)		
Mean±s.d.	0·88±0·9	3·0±1·2
Range	0–3	2–6

The blood lost in the patients given SNP was only 40 per cent of that lost by controls and the transfusion requirement was also lower. To check against the anaesthetist's bias 'in favour' of the SNP group—she, of necessity, knew which patients were receiving the drug—we compared the 48 h postoperative haemoglobin levels with those at the pre-operative stage as a crude indicator of blood replacement. These values rose in both groups by a comparable amount and this suggests that the SNP patients were not deliberately undertransfused. Sodium nitroprusside also lowered the portal pressure slightly, but the systemic arterial pressure was reduced more and both these measurements were related significantly to blood loss. It is not possible however to state which pressure reduction was the more important.

We did not find reactionary haemorrhage to be greater in patients receiving SNP, and this has also been the experience of others[7]. In our procedure the hypotension was reversed 15 min before closure was begun, as this precaution lessens the risk of postoperative bleeding.

Renal damage due to hypotension has not been reported with SNP[6] as the drug results in renal artery dilatation and we noted an increased urine output despite hypotension.

Other dangers of SNP use include severe hypotension from too rapid administration and cyanide toxicity when doses over 1·5 mg/g are used[2,6]. The latter complication is generally preceded by metabolic acidosis[8]. These complications are rare and can be avoided by careful monitoring of the patient and attention to detail.

Currently SNP is the drug of choice for inducing controlled hypotension during anaesthesia. It produces a consistent hypotension that is easily induced and reversed[2], it lacks a depressant action on the heart and the incidence of tachyphylaxis is low. This drug dilates the coronary, pulmonary, and renal arteries, but its action on the portal venous system has not been well defined[2]. We found that it lowered portal pressure slightly but this fall did not have any lasting deleterious effect on liver function. Others[6,8] have also found that liver function was unaltered when SNP was used.

In view of our findings of its apparent safety, SNP hypotensive anaesthesia may be used more widely in operations for portal hypertension where liver function is preserved. The reduction of blood requirement has important implications in many countries as it means that operations can be performed in hospitals where blood for transfusion is scarce.

References

1. Nundy S, Tandon BN. *Portal hypertension in India*. New Delhi, Rajgarhia Clinical Liver Research Unit, AIIMS, 1978.
2. Kreye VAW. Sodium nitroprusside. In: Scriabine A, ed. *Pharmacology of Antihypertensive Drugs*. New York: Raven Press, 1980: 373–92.
3. Smith DL, Didier EP, Clagett OT. Controlled hypotension in radical mastectomy: second 5 year review. *Ann Surg* 1966; **163**: 263–6.
4. Enderby GEH. Some observations on the use of hypotensive anaesthesia. *Brit J Anaesth* 1975; **47**: 747–8.
5. Gupta AK. Blood loss in major surgical procedures. *Indian J Surg* 1983; **41**: 266–72.

6. Verner IR. Direct acting vasodilators. In: Enderby GEH, ed. *Hypotensive Anesthesia*. New York: Churchill Livingstone, 1985: 139–51.
7. Lindop MJ. Complications and morbidity of controlled hypotension. *Brit J Anaesth* 1975; **47**: 799–803.
8. Tinker JH, Michenfelder JD. Sodium nitroprusside: pharmacology, toxicology and therapeutics. *Anesthesiology* 1976; **45**: 340–54.

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Surgical workshops

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Electronic device for the detection of breaches in asepsis during surgical procedures

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The provision of a microbiologically clean environment in which to operate is one of the most influential factors in the outcome and success of many surgical procedures. Cotton gowns and drapes are not impervious to organisms, particularly when they are wet[1], hence the advice that waterproof drapes and gowns should be used in cases where asepsis is crucial. Organisms derived from the skin of the surgeon soon appear within surgical gloves, and Devenish and Miles were the first to report the threat that a punctured glove may have to the sterility of a patient's wound[2]. Glove punctures are often minute and may not be felt by the surgeon when they occur. Nevertheless, such minute holes are capable of allowing organisms to pass through, so it would seem desirable to be able to warn a surgeon, as soon as a puncture occurs, to stop operating and change his gloves. This is of importance not only for asepsis but also when operating on patients carrying the hepatitis B or HIV virus.

Materials and methods

The electrical resistance between surgeon and patient during an operation should be extremely large, approaching infinity. The surgeon should be insulated from the patient by his gown, the drapes, and in particular by his gloves. When the gown or drapes become wet, or a glove is punctured during a case, an 'electrolyte bridge' forms between the surgeon and patient, and the resistance between the two falls, allowing current to flow. The operation of the device described (*Figure 1*) here depends upon a fall in this resistance. A standard ECG electrode is attached to the surgeon in any comfortable position, the diathermy plate being used as the patient's connection, allowing continuous monitoring of resistance between the two during a case. In the event of the patient–surgeon resistance falling, an audible alarm is activated.

A determination of the electrical resistance through a glove puncture, as an indication of the likely resistance resulting from a breach of the aseptic barrier, was made to enable the sensitivity of the detector circuit to be set accordingly. This was achieved using a sensitive ohmmeter connected between an ECG electrode attached to a subject's back and to the side of an aluminium bowl containing warm saline. A glove was then placed on the subject's hand and a pinprick made on the tip of the index finger. The gloved hand was then placed into the bowl.

Initially the resistance appeared to be infinite but, as saline entered the glove over approximately 60 s, it fell. When an area of finger approximately 5 × 5 mm was covered with saline the resistance was 1 MΩ; as more fluid entered the resistance fell quickly to <500 kΩ.

A 'dry' perforation has a resistance in excess of 4 MΩ and may be unlikely to provide a route for organism transfer; 1 MΩ was therefore chosen as the resistance below which the alarm should be triggered. A determination of the resistance between the surgeon and patient through a damp patch on the drapes or gown was not made, but it probably is <1 MΩ if a significant area of gown is involved; such an area would be many times the cross-sectional area of a glove puncture, the resistance being proportionately lower.

The circuit used is based on an operational amplifier (IC Type LM307N.STC Electronics Services) whose gain is adjusted by the variable resistor between pins 3 and 6 (*Figure 1*). The surgeon's electrode is attached to terminal 'A', the patient's to 'B'. If the resistance between A and B falls below 1 MΩ, a small current flows between the two (about 9 μA), and pin 6 of the operational amplifier falls to 0 V, sounding the buzzer. In the event of the alarm sounding, the circuit can be reset by pushing the button shown. The 0·1 μF capacitor across A and B smooths any transient currents that may arise from electrical equipment in theatre, that may not be attached to the patient, and prevents the circuit being set off by diathermy use. The possibility exists that if the diathermy return plate became detached, with this circuit's electrode still in place on the patient, radio frequency current might leak through this circuit to the surgeon and possibly burn him. The problem is eradicated by having the diathermy return plate as a common patient electrode for both circuits. The maximum current flow that is allowed for monitoring equipment attached to the skin of a patient, as defined by British Standard 5724, is 100 μA[3]. At a current flow of 9 μA, this circuit is well within that figure.

The device is enclosed in a small plastic box that can be placed well away from the operating table, and all the surgeon has to endure is the ECG electrode. Long leads are used to allow the surgeon maximum mobility.

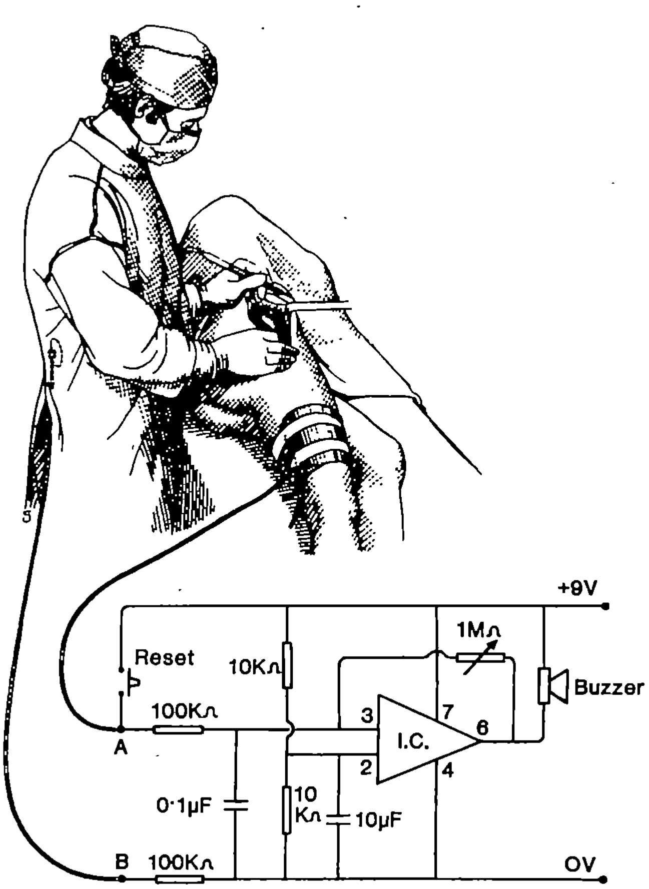

Figure 1 *Diagram to show the circuit and its connections to the surgeon and patient. The integrated circuit (IC) is type LM307N, resistances are quoted in kΩ or MΩ and capacitance in μF. The circuit is enclosed in a small plastic box and cost approximately £10 to build*

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Discussion

The device had undergone initial testing during ten surgical cases consisting mainly of routine orthopaedic procedures where the surgeons were taking due care to maintain asepsis. It proved capable of detecting glove punctures on three occasions, of which the surgeons were unaware, and on three other occasions warned of wet patches on surgeons' gowns which were small enough not to alert them. In none of the ten cases described did the surgeons complain of inconvenience caused by the device.

Acknowledgements

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References

1. Moylan JA, Kennedy BV. The importance of gown and drape barriers in the prevention of wound infection. *Surg Gynecol Obstet* 1980; **151**: 465–70.
2. Devenish EA, Miles AA. Control of staphylococcus aureus in an operating theatre. *Lancet* 1939; i: 1088–94.
3. British Standards Institution. Medical electrical equipment. BS 5724: Part 1: Specification for general safety requirements. London: British Standards Institution, 1979.

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Technique for intra-operative colonic irrigation

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Intra-operative colonic irrigation provides a suitable environment for primary anastomosis after emergency left-sided colonic resection and the technique is gaining ground in surgical practice[1–3]. If it is to be used safely, great care must be taken to ensure that faecal soiling is kept to a minimum. A technique and equipment, specifically designed to facilitate colonic irrigation with minimal contamination, are described.

Equipment and technique

The equipment comprises a one-piece disposable polythene bag for collecting faecal effluent and a Verres-type needle for introducing the irrigating fluid. The bag has a capacity of 7 litres and is attached to a flexible conduit 1 m in length, with a rigid tube of 3·5 cm diameter leading into the conduit (*Figure 1*). The tube is introduced into the colon, either through a colotomy immediately proximal to the obstructing lesion or through the proximal divided end after resection, and is tied in place using braided ligature material passed around the bowel. The tube has two circumferential ridges which allow firm placement of double ligatures, thus minimizing the risk of dislodgement and leakage. The irrigation device consists of a hollow needle 3 mm in diameter and a spring-loaded hollow obturator with a distal side hole (*Figure 2*). The obturator, which slides into position when the spring is released, is directly connected to a standard intravenous fluid administration set via a luer-lock system.

Once the disposal system is in place (*Figure 3*) and before irrigation, the proximal colon is gently manipulated to displace most of its contents into the reservoir. It is easier to empty the colon if the splenic flexure is mobilized. The needle, with the obturator disengaged, is then introduced into the terminal ileum by direct puncture. The obturator is released and the needle advanced through the ileocaecal valve into the caecum. The needle can be held in place using a suture inserted into the ileal wall and tied around a purpose made groove in the needle hub. Lavage, with 3–6 litres 0·9 per cent saline warmed to 37°C, and manipulation of the colon to break down any remaining solid faeces within the colon provides adequate preparation for an immediate bowel anastomosis. When the needle is withdrawn at the end of the procedure the small puncture wound is easily closed with one or two sutures.

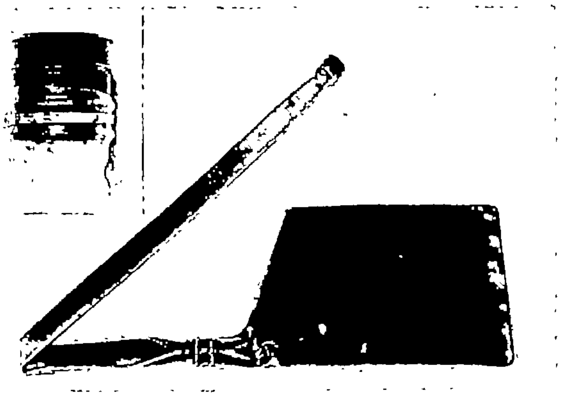

Figure 1 *Colonic irrigation bag. Inset shows ridged introduction tube*

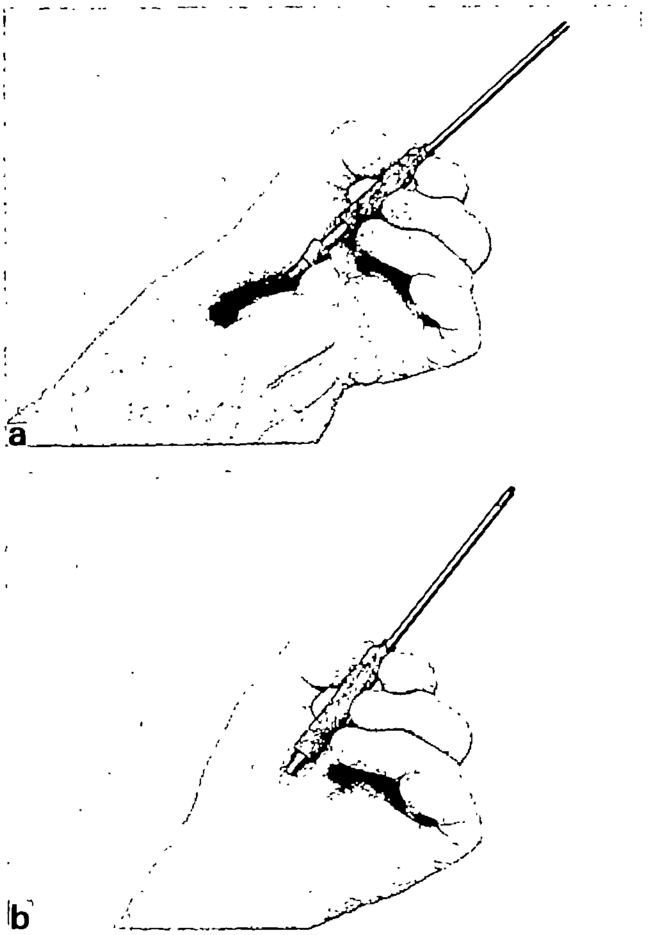

Figure 2 , *Verres-type irrigation needle with obturator withdrawn;* **b**, *needle with obturator in place*

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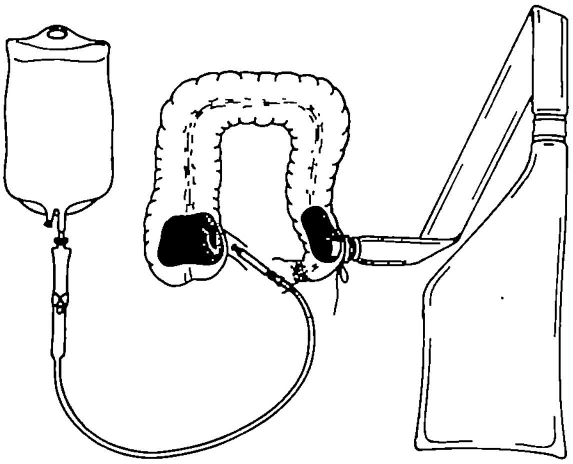

Figure 3 *Diagram of irrigation bag and needle in use*

Discussion

Faecal loading is a major causative factor in colonic anastomotic dehiscence[4-6] and, even in elective surgery, preoperative preparation of the large bowel can be unsatisfactory regardless of the method used[7]. Intra-operative mechanical cleansing of the colon can overcome this problem and there are now reports of good results following primary colocolic or colorectal anastomosis preceded by on-table colonic preparation, both in elective and emergency situations[1-3,8-9].

Muir[8] performed colonic cleansing through a wide bore glass tube inserted into a colotomy proximal to the obstructing lesion. This was supplemented by antegrade lavage via a separate caecostomy or retrograde irrigation through the glass tube itself. Thow[9] described a complex method of lavaging the proximal colon by means of a long tube inserted along the whole length of the small intestine and through the ileocaecal valve. The most satisfactory method to date is that described by Dudley and his colleagues[10], whereby antegrade colonic irrigation is performed through a size 14 Foley catheter inserted into the caecum, the effluent being collected by anaesthetic gas scavenging tubing tied into the distal large bowel. This technique has been usefully employed in at least three reported series[1-3], but it can be difficult to perform without incident. Solid faecal material may become lodged in the scavenging tube and minor degrees of faecal spillage are difficult to avoid.

We believe that the method and purpose-designed equipment described here offer considerable advantages during intra-operative colonic preparation. The irrigation needle provides a means of introducing the lavage fluid into the caecum with minimal contamination. The disposal bag is similarly designed to reduce the risk of faecal leakage and, unlike more rigid tubing, blockage of the flexible conduit can be overcome by manipulation.

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References

1. Radcliffe AG, Dudley HAF. Intra-operative antegrade irrigation of the large intestine. *Surg Gynecol Obstet* 1983; **156**: 721–3.
2. Koruth NM, Krukowski ZH, Youngson GG *et al.* Intraoperative colonic irrigation in the management of left-sided large bowel emergencies. *Br J Surg* 1985; **72**: 708–11.
3. Thomson WHF, Carter SStC. On table lavage to achieve safe restorative rectal and emergency left colonic resection without covering colostomy. *Br J Surg* 1986; **73**: 61–3.
4. Irvin TT, Goligher JC. Aetiology of disruption of intestinal anastomoses. *Br.J Surg* 1973; **66**: 461–4.
5. Schrock TR, Deveney CW, Dunphy JE. Factors contributing to leakage of anastomoses. *Ann Surg* 1973; **177**: 513–18.
6. Smith SRG, Conolly JC, Gilmore OJA. The effect of faecal loading on colonic anastomotic healing. *Br J Surg* 1983; **70**: 49–50.
7. Keighley MR. Clinical and physiological evaluation of bowel preparation for elective colorectal surgery. *World J Surg* 1982; **6**: 464–70.
8. Muir EG. Safety in colonic resection. *Proc R Soc Med* 1968; **61**: 401–8.
9. Thow G. Emergency left colon resection with primary anastomosis. *Dis Colon Rect* 1980; **23**: 17–24.
10. Dudley HAF, Radcliffe AG, McGeehan D. Intra-operative irrigation of the colon to permit primary anastomosis. *Br J Surg* 1980; **67**: 80–1.

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The colonic irrigation bag is available from: Tuta Laboratories, 318–332 Burns Bay Road, Lane Cove, New South Wales 2066, Australia. The irrigation needle is available from: Northern Hospital Supplies, 41 Spylaw Street, Colinton, Edinburgh EH13 0JT, UK

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Thermogenesis after major elective surgical procedures

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Sequential changes of body temperature have been measured for 48 h in 147 patients after major elective abdominal, cardiac, orthopaedic and pelvic surgery. Core temperature (aural canal) started to increase immediately after surgery reaching a mean peak value of 37·5°C 14 h (range 8–16) after the end of surgery. Subsequently, a second peak of 37·4°C was shown 18 h (range 16–20) later. The time interval between these two peak temperatures was constant for all types of surgery studied. A close examination of core temperature oscillations during a 72-h postoperative period and a comparison with a pre-operative 24-h cycle in a group of 14 patients who underwent cardiac surgery did not show any circadian rhythm. In the third part of the study, analysis of postoperative body temperature and metabolic rate showed a similar pattern of increase for core and mean skin temperatures, and oxygen consumption.

Keywords: Temperature, operation, thermogenesis, metabolic rate, circadian rhythm

Fever is a highly integrated biological response and one of the most commonly observed clinical signs of disease. The presence of fever following surgical injury is an accepted phenomenon and regarded as a physiological response to a pathological process.

Cuthbertson[1], in 1942, introduced the terms ebb and flow to describe the immediate and later phases of the response to injury. The ebb phase was characterized by a reduction, and the flow phase by an increase, in body temperature.

It was decided to undertake the present study in order to describe more critically the pattern of thermogenesis during the postoperative period, to examine the oscillation of body temperature during this time and finally to analyse the redistribution of body heat and its relationship with the metabolic rate during the first 24 h after surgery.

Patients and methods

One hundred and forty-seven adult patients undergoing abdominal, pelvic, cardiac or orthopaedic surgery were studied. They were divided into three groups which were studied at different times. The first group (A) included 97 patients who underwent abdominal, pelvic or orthopaedic surgery. In these patients body core temperature was recorded every 2 h for two postoperative days. In the second group (B) of 14 patients, who underwent coronary artery bypass graft, core temperature was recorded every 2 h, for 1 day before and 3 days after surgery to analyse the pattern of circadian rhythm. In the third group (C) of 36 patients, who underwent abdominal, pelvic or orthopaedic surgery, core and mean skin temperatures were recorded and metabolic rate measured before and every 4 h for 24 h after surgery.

Patients with a metabolic disorder, endocrine diseases or a pre-operative pyrexia were not included in the study. Informed consent was obtained in each case. On the day before surgery the skinfold thicknesses and mid-arm circumference were measured to calculate the ratio of fat to body weight[2]. The duration of pre-operative starvation was also recorded.

Anaesthesia and surgery

The patients were premedicated with papaveretum and hyoscine administered by intramuscular injection 90 min before surgery. General anaesthesia was achieved with thiopentone 5 mg kg^{-1}, suxamethonium 1 mg kg^{-1}, pancuronium 0·1 mg kg^{-1} or *d*-tubocurarine 0·5 mg kg^{-1}, fentanyl and halothane or enflurane. The lungs were ventilated to normocapnia with a mixture of nitrous oxide in oxygen. Local anaesthesia, when used, consisted of either a lumbar, subarachnoid or epidural block using either cinchocaine or bupivacaine. The height of the block was assessed by pin prick aiming to establish analgesia to the level of the tenth thoracic dermatome.

Elective major surgical procedures included 46 abdominal, 40 pelvic, 14 cardiac and 47 orthopaedic operations. Patients were scheduled for either morning or afternoon surgery. Moderate hypothermia (28°C) and non-pulsatile perfusion were used for cardiac surgery. Rewarming, in this group, was commenced on release of the aortic cross-clamp and continued until the aural canal temperature reached 37°C.

All patients received, intra-operatively, an intravenous infusion of Hartmann's solution at a rate of 4 ml kg^{-1} h^{-1} and after surgery a mixture of 4 per cent dextrose in 0·18 per cent sodium chloride at a rate of 40 ml kg^{-1} 24 h^{-1} until they were able to tolerate oral fluids. When blood loss was over 20 per cent of the circulating blood volume it was replaced with dextran 70 in sodium chloride. Only patients who underwent cardiac surgery received blood transfusion. At the end of surgery patients were admitted to the recovery room for 1 hour before being transferred to their wards.

Those who underwent cardiac surgery were transferred to the intensive care unit where they artificially ventilated for 8 h until they were haemodynamically stable.

Postoperative pain relief was achieved with an intramuscular injection of papaveretum, 0·25 mg kg^{-1} as required. Three doses of prophylactic antibiotic, either cefuroxime or cephradine, were administered intravenously perioperatively to all patients. Blood cultures were taken daily before and after surgery and, when positive, the patients were excluded from the study.

Temperature measurements

After induction of anaesthesia a thermocouple probe was inserted under direct vision in the aural canal and well secured with cotton wool to avoid draughts. This site was chosen because it is well tolerated by the patient, easily inserted and does not cause trauma. Provided steps are taken to avoid draughts and cold air, aural canal temperature correlates well with oesophageal temperature[3]. In group C, skin surface probes were applied to the chest, arm, thigh and calf to measure mean skin temperature. Body temperature measurements were taken before and at the end of surgery, and subsequently every 2 or 4 h for either 2 or 3 days. All the probes and the thermometers were manufactured by Cormack Electronics and were calibrated against a National Physics Laboratory (NPL) mercury in glass thermometer. They were accurate to 0·05°C over the temperature range studied.

Ambient temperature and relative humidity were measured in the operating theatres and in the postoperative wards by means of a mercury in glass thermometer and a hair hygrometer respectively (Negretti and Zambia). Mean skin temperature was calculated using the formula proposed by Ramanthan[4] where mean skin temperature $= 0{\cdot}3(T_{\text{chest}} + T_{\text{arm}}) + 0{\cdot}2(T_{\text{thigh}} + T_{\text{calf}})$. This method has been compared with the other 11 different formulae described by several

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authors to the 15-site reference value[5]. According to the author the 4-points formula reaches a 95 per cent agreement to within 1°C of the mean skin temperature during anaesthesia. Holdcroft and Hall[3] compared the 15-site method of Mitchell and Wyndham[6] with the 4-point method during anaesthesia and recovery and found sufficient agreement.

Mean body temperature was calculated by averaging mean skin and core (aural canal) temperatures according to the equation of Colin *et al.*[7], mean body temperature $= 0{\cdot}66T_{\text{core}} + 0{\cdot}34T_{\text{mean skin}}$. Body heat content (kJ) was calculated[8], and corrected for body weight. Total body heat = mean body temperature × body weight × 0·83 × 4·1868.

Gas exchange measurements

These were performed by the open circuit method of indirect calorimetry before and after surgery. The measurements were performed with the patients resting in the supine position and breathing room air. To minimize hyperventilation during gas collection, all patients underwent a period of adaptation to breathing through a mouthpiece with a non-breathing valve and the nasal airway occluded with a nose clip. This period of adaptation was continued until the patients reached a steady state as measured by the end-tidal and mixed expired carbon dioxide. Measurements of gas exchange were started 4 h after the end of surgery. The reasons for the delay were the unstable cardiorespiratory system and the recovery from the effect of the anaesthetic gases occurring during the immediate postoperative period which might interfere with the measurement and the results.

Expired gases were passed through a modified mixing device system previously described[9], which consisted of four 1-litre reservoir bags connected in series. The first two bags were each filled with pieces of nylon and the third and fourth were fitted with a sampling tube and tap. Expired gases were collected for three periods of 3 min each and measured with a dry gas meter (T. Glower, Edmonton), previously calibrated against a Tissot spirometer and found to be accurate to within 0·10 litre in 10 litres.

The concentrations of inspired (F_I) and mixed expired ($F_{\bar{E}}$) oxygen were measured by a paramagnetic analyser, Servomex type OA101 MK II, precalibrated with 99·8 per cent nitrogen in air and room air. The concentration of mixed expired ($F_{\bar{E}}$) carbon dioxide was recorded by an infra-red carbon dioxide analyser (Hewlett Packard), the calibration of which was repeatedly checked with pre-analysed gas mixtures of 3 and 5 per cent carbon dioxide in oxygen.

Oxygen consumption (l min^{-1}) was determined from the minute volume and gas concentration according to the formula:

$$\dot{V}_{O_2} = \dot{V}_I(\text{STPD}) \times F_{I,O_2} - \dot{V}_E(\text{STPD}) \times F_{\bar{E},O_2}$$

Inspired ($\dot{V}_I$) and expired ($\dot{V}_E$) minute volumes were considered to be equal and corrected for standard temperatures (0°C) and atmospheric pressure (P_{atm}, 760 mmHg) dry (STPD).

$$\dot{V}(\text{STPD}) = \dot{V}(\text{ATP}) \times \frac{P_{\text{atm}} - P_{\text{water}}}{760} \times \frac{273}{273 + T_{\text{ambient}}}$$

where ATP is the ambient temperature and pressure, saturated with water vapour; P_{water} is the water vapour pressure measured at the time of the experiment; T_{ambient} is the environmental temperature measured at the time of the experiment; and 273 is absolute temperature.
Carbon dioxide production (l min^{-1}) was determined from the minute volume and gas concentration according to the formula:

$$\dot{V}_{CO_2} = \dot{V}_E(\text{STPD}) \times F_{\bar{E},CO_2}$$

For all patients studied, the reproducibility of three observations during each period was better than 5 per cent. The coefficient of variation was 3·7 per cent.

Resting energy expenditure (REE), expressed as a function of body weight, was calculated according to Weir's formula[10]:

$$\text{REE}(\text{kJ h}^{-1}) = 3{\cdot}94 \times \dot{V}_{O_2} + 1{\cdot}1 \times \dot{V}_{CO_2} \times 60$$

Indirect calorimetry utilizes oxygen consumption, carbon dioxide production and nitrogen excretion as a measure of heat production; the latter results from oxidation of carbohydrate, fat and protein. Under some circumstances it is possible to neglect the protein component and Weir[10] suggested that the calorific value of expired air may be used as a constant with measurements of its volume only. There are many studies that show excellent correlation between direct and indirect calorimetry when carried out simultaneously[11].

Statistical analysis

For each patient, the rate of change in temperature was calculated as the slope of the regression line of body core temperature on time (0, 2, 4, 6, 8, 10, 12, 14, and 16 h). This value was used as the dependent variable in the stepwise multiple regression analysis which determined the factors which were independently correlated with the rate of change. Student's unpaired and paired *t* tests were used when appropriate. Results are represented by mean (±s.d. or s.e.m.) and a statistically significant change was considered to have occurred when *P* values were 0·05 or less.

To analyse postoperative core temperature rhythm and compare it with a 24-h pre-operative pattern (circadian rhythm), a mean value of body temperature over a 12-h period (12.00–24.00 and 24.00–12.00 hours) was obtained for each patient before and after surgery and analysis of variance applied.

Results

The demographic details of all patients studied are shown in *Table 1*. The pelvic surgery included only female patients undergoing gynaecological operations with a mean age lower than the other surgical groups. The details related to duration of surgery, pre-operative starvation time, type of anaesthesia used and blood loss for each type of surgery (*Table 2*) were statistically different from those of the other three surgical groups. Mean ambient temperature in theatre was 20·7°C (range 19·5–22·5) and in the wards 25·0°C (23·1–26·7). Mean relative humidity was 53 per cent in theatre and 40 per cent in the wards.

Group A (97 patients)

Mean core body temperatures of the first group of 97 patients studied are graphically represented in *Figure 1*. From the analysis of all data and for each of the three types of surgery, a peak mean temperature of 37·5°C was reached 14 h (range 8–16) after the end of surgery and the mean rate of temperature changes per hour was 0·17°C. A second peak of 37·4°C was shown 32 h (range 30–34) after the end of the operation. The overall incidence of shivering was 26 per cent, and was largely detected in patients under 60 years of age after general anaesthesia.

Group B (14 patients)

The 24 h pre-operative and 72 h postoperative mean core temperatures of 14 patients who underwent coronary artery bypass graft surgery are represented in *Figure 2*. In this group a peak mean core temperature of 37·8°C was reached 12 h after the end of surgery. Postoperative mean temperatures were higher ($P < 0{\cdot}05$) than those recorded during the 24-h period

Table 1 *Characteristics of study subjects*

Type of surgery	Abdominal (*n*=46)	Pelvic (*n*=40)	Cardiac (*n*=14)	Orthopaedic (*n*=47)
Age (years)	55 (41–72)	36 (25–49)	55 (47–65)	48 (24–63)
Sex M:F	28:18	0:40	9:5	27:20
Weight (kg)	64·3±12·1	65·7±12·1	73·9±14·5	68·7±11·1
Height (cm)	170·1±7·8	167·3±4·7	172·1±9·4	168·8±7·5
Body fat (%)	33·5±4·7	35·7±2·1	32·6±1·9	32·9±3·3

The median and range of subjects' ages are given. Values for weight, height and body fat are means±1 s.d.

Table 2 *Clinical data*

Type of surgery	Abdominal ($n=46$)	Pelvic ($n=40$)	Cardiac ($n=14$)	Orthopaedic ($n=47$)
Duration of surgery (min) Mean ± 1 s.d.	146·2 ± 47·8	121·1 ± 25·9	205·7 ± 14·5*	111·0 ± 18·9
Starvation time (h) Mean ± 1 s.d.	17·3 ± 3·5	15·5 ± 2·7	16·1 ± 1·6	17·8 ± 1·8
Type of anaesthesia				
(general)	46	32	14	29
(regional)	—	8	—	18
Blood loss Median (range)	361 (123–579)	277 (150–460)	1890* (1410–2320)	325 (110–625)

* Significantly different from other groups ($P<0·05$)

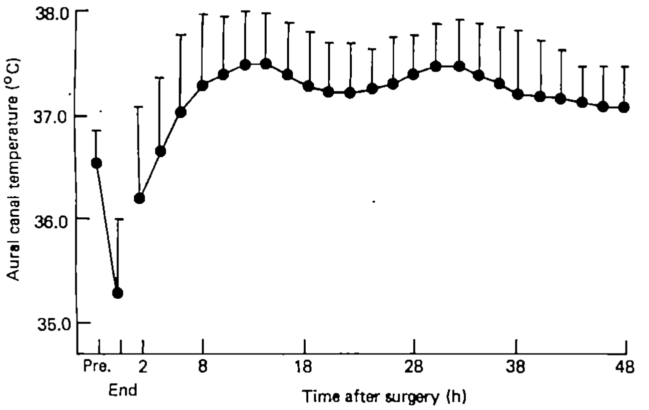

Figure 1 *Mean (± 1 s.d.) cumulative aural canal temperatures of 97 patients recorded before and at the end of surgery, and subsequently every 2 h for 48 h*

before operation. However, when attempts were made to compare those with the 12-h pre-operative period rhythm (high core temperature between 12.00 and 24.00 hours and low core temperature during 24.00 and 12.00 hours) no oscillatory patterns were shown.

Group C (36 patients)

The measurements of core, mean skin and mean body temperatures of this group of patients who underwent either abdominal, pelvic or orthopaedic surgery are represented in *Figure 3*. During the first 12 h there was an increase in core and mean skin temperature. The increase in mean body temperature and calculated body heat content during this period of time was 8 per cent (range 6–11). Similarly, the amount of oxygen consumed and carbon dioxide produced increased ($P<0·05$) in the first 24 h (*Table 3*) and the calculated resting energy expenditure increased by 30 per cent above the control value 16 h after the end of surgery (*Figure 4*). The rise in mean body temperature correlated with the rise in metabolic rate only for the first 12 postoperative hours. The latter continued to rise and remained high for the whole of the 24-h period.

Discussion

The first part of this study (group A) showed that core temperature increased immediately after surgical trauma and reached a peak value within 14 h after the end of surgery. This increase occurred independently of the type and degree of surgical trauma. In addition, a biphasic febrile response was observed during the first 48 h of core temperature measurements with a second peak occurring 32 h after the end of surgery. In all three types of surgery the interval between the two peaks remained fairly constant.

The rise in core temperature in the immediate postoperative period was almost linear except in the orthopaedic group where the peak temperature occurred 16 h after the end of surgery. The reason for this slower rate of temperature change might be that 18 out of 47 patients in this group received a regional block as an anaesthetic technique, and therefore, as shown previously[12], motor and sympathetic blockade might have delayed the immediate postoperative rewarming. From our results the rate of increase of body temperature during the first 16 h was related neither to the demographic characteristics of the patients, nor to the duration of surgery. However, the female patients in the pelvic group, with a mean age of 38·7 years, reached a peak temperature faster (10 h) than the other groups. It might be possible that this fast rate of change in core temperature occurred in the immediate recovery period when age seems to be an important factor[12].

In studies on the pathophysiology of injury, the surgical model has been extensively used and many metabolic similarities with other types of injury have been found. Cuthbertson[1], in his original observations, described an immediate or ebb and a later or flow phase of the response to injury. The ebb phase was characterized by a reduction in body temperature and metabolic activity, lasting some time, followed by a flow phase during which heat production and metabolism increased.

The fall in body temperature has been described in rats after limb ischaemia or scald by Stoner[13], who showed that, at ambient temperature below the thermoneutral zone, body temperature and energy production were reduced as a result of central inhibition of thermoregulation. The thermoneutral zone was extended after injury and the critical temperature for the onset of thermoregulatory heat production was reduced. In man the fall in body temperature seems related to the severity of injury, however the evidence of ebb phase is equivocal[14].

From our data collected after major elective surgical procedures there is no evidence of the postoperative ebb phase. Indeed, the increase in core temperature in this study started in the immediate recovery period. It might be that the physiological disturbances occurring with surgery were promptly treated (anaesthesia, oxygenation and substrates—fluids, calories—provided) and therefore the ebb phase, as described by Cuthbertson[1] after bone fracture, was absent. One might assume that the intra-operative fall in body temperature could be counted as an ebb phase, however it has been observed that, in patients whose perioperative body temperature was actively maintained at pre-operative values, the postoperative body temperature increased to the same levels described in this study (F. Carli, unpublished observations). The mechanism of the increase in body temperature during the postsurgical period is not clear. It cannot be explained on the basis of a peripheral cold stimulus as mean skin temperature as well as core temperature was rising (group C) (*Figure 3*). Similar findings were shown during the flow phase of thermal injury[15]. Therefore heat production during this period might be secondary to a change in thermoregulatory control.

Protein catabolism has been discussed but it seems unlikely to be the complete explanation. The role of hormones on heat production has been recently reconsidered following the study by Bessey *et al.*[16], who infused, simultaneously, glucagon,

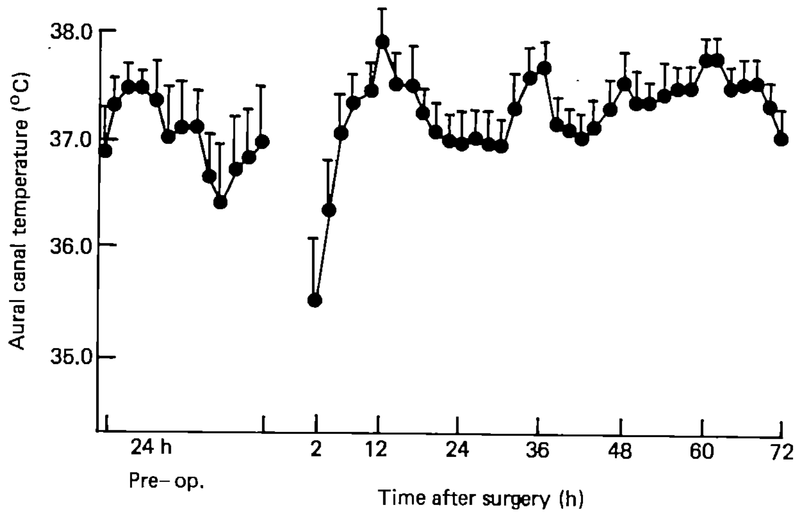

Figure 2 *Mean aural canal temperatures of 14 patients (±1 s.d.) who underwent coronary artery bypass graft recorded every 2 h for 24 h pre-operatively and 72 h postoperatively*

Table 3 *Pre- and postoperative* O_2 *consumption* ($\dot{V}_{O_2}$), CO_2 *production* ($\dot{V}_{CO_2}$) *and respiratory quotient* (*R*)

	Before surgery	After surgery (h)					
		4	8	12	16	20	24
$\dot{V}_{O_2}$ l min^{-1}	0·164 ± 0·053	0·169 ± 0·042	0·187 ± 0·044	0·212 ± 0·040	0·218* ± 0·057	0·193 ± 0·045	0·208 ± 0·048
$\dot{V}_{CO_2}$ l min^{-1}	0·147 ± 0·049	0·148 ± 0·045	0·165 ± 0·039	0·184 ± 0·033	0·191* ± 0·047	0·169 ± 0·036	0·184 ± 0·043
R	0·89 ± 0·05	0·89 ± 0·07	0·88 ± 0·05	0·86 ± 0·05	0·87 ± 0·06	0·88 ± 0·06	0·89 ± 0·07

Values are mean ± 1 s.d. * Significantly different from pre-operative value ($P < 0·05$)

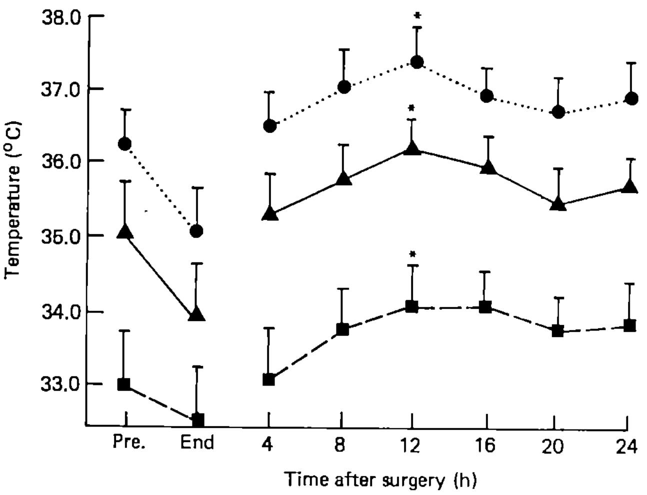

Figure 3 *Aural canal* (●), *mean body* (▲) *and mean skin* (■) *temperature* (±*1 s.d.*), *recorded before and at the end of surgery, and subsequently every 4 h for 24 h in 36 patients who underwent major elective abdominal, orthopaedic or pelvic surgery. The rate of change of aural canal temperature was faster than that of mean skin during the first 12 h after operation.* **Significantly different from pre-operative values* ($P < 0·05$)

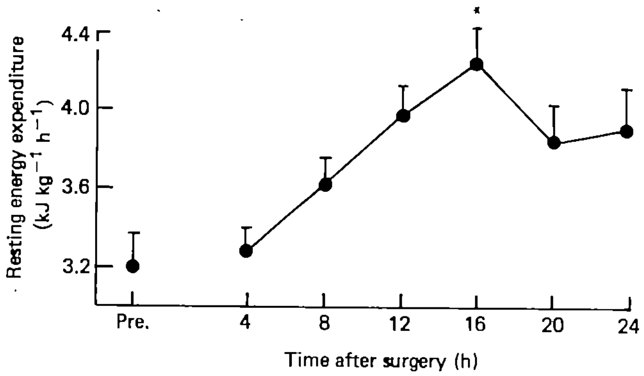

Figure 4 *Mean resting energy expenditure (±1 s.e.m.) measured before and every 4 h for 24 h after surgery in 36 patients.* * *Significantly different from pre-operative values* ($P < 0·05$)

cortisol and adrenaline in human volunteers for 3 days and were unable to show a significant increase in body temperature. More recently the role of polypeptide interleukin (IL-I), also called leucocyte pyrogen, has been considered[17]. This low molecular weight compound may be responsible for several apparently unrelated changes observed after surgery. These include acute phase protein synthesis in the liver[18], T lymphocyte proliferation, antibody formation, release of neutrophils from bone marrow, muscle proteolysis and, among others, the febrile response to trauma. The increase in concentration of the acute proteins which occurs several hours after injury[19,20], is related to the presence of the products of tissue damage that stimulate the macrophages to produce IL-I which causes the liver to switch on the synthesis of the acute phase proteins. Of the proteins, C-reactive protein (CRP) shows the most rapid increase after surgery and this increase correlates very well with that of body temperature.

The second observation in the first part of this study was the biphasic febrile type response with two peaks during the first 48 hours of core temperature measurements. The mechanism of this type of response is, at present, not clear. A circadian rhythm is excluded because the 97 patients in group A were operated on at different times during the day. A possible explanation of this phenomenon comes from the experimental work on intravenous administration of exogenous pyrogen to rabbits which produced endogenous pyrogen capable of causing a biphasic fever with a fairly constant interval between two peaks. Therefore endogenous pyrogen might behave as activator and product of this febrile response[21].

From the analysis of the core temperature, the interval observed between the two peaks occurred regularly in all patients despite the timing of surgery. It was therefore decided to investigate further this aspect by recording pre- and postoperative body core temperature of patients undergoing cardiac surgery (group B). This type of surgery, despite the blood transfusion, was chosen because it represents a model of major surgical trauma involving severe cardiorespiratory and metabolic changes. When we compared the patterns of postoperative core temperatures with those recorded preoperatively, no oscillatory pattern was observed in the first 3 days after surgery. Moore-Ede *et al.*[22] and Bell *et al.*[23] have shown an altered or lost pattern of circadian rhythm following trauma. The importance of this is not known, however, if abnormal rhythms were to be considered as undesirable as they are in shift workers and trans-meridian travellers, it is possible that the postsurgical prognosis might be affected. At present we are investigating a possible technique of recording core temperature for long periods of time and further studies are needed in this field.

In the third part of this study (C), 36 patients who underwent major abdominal, pelvic or orthopaedic surgery were studied with the intent of looking at the redistribution of body heat during the first 24 h after surgery and its relationship with the metabolic rate. Core and mean skin temperatures (*Figure 3*) and the calculated total body heat content increased following surgery, and reached a peak at the 12th hour after the end of surgery.

Therefore the change in core temperature after surgical trauma did not seem to be the result of peripheral vasoconstriction as described by Little and Stoner[14] in 82 patients after accidental injuries. While a fall in mean skin temperature was attributed by them to vasoconstriction, that of core temperature was due to decreased heat production. Postoperative metabolic rate or energy expenditure in our study increased by 30 per cent above the pre-operative value and this might seem in contrast with the 5–8 per cent observed by Kinney and Roe[24] during the first postoperative week. However our data are related to sequential changes during the first 24 h.

Another interesting observation was the discrepancy between the rises in heat content or mean body temperature and energy expenditure. We do not have an explanation for this, however, the work of Bessey *et al.*[16] showed that the metabolic rate increased significantly following the infusion of hormones with no relevant changes in body temperature.

While some authors claimed that exposure to a warm and dry environment decreases hypermetabolism after injury[25], others have been unable to prove this[26]. When these manipulations of body temperature have been adopted perioperatively a beneficial effect on postsurgical protein metabolism has been shown[27,28]. Further studies on energy production in the postsurgical model are needed.

As suggested by Kinney[29], measurement of sequential changes of resting energy expenditure after surgery can give useful information in order to define the level of hypermetabolism necessary to recover and to intervene with adequate support of circulation, respiration and nutrition when this level might be undesirable.

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References

1. Cuthbertson DP. Post shock metabolic response. *Lancet* 1942; **I**: 433–7.
2. Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged 16 to 72 years. *Br J Nutr* 1974; **32**: 77–97.
3. Holdcroft A, Hall GM. Heat loss during anaesthesia. *Br J Anaesth* 1978; **50**: 157–64.
4. Ramanathan NL. A new weighing system for mean surface temperature of the human body. *J Appl Physiol* 1964; **19**: 531–3.
5. Shanks CA. Mean skin temperature during anaesthesia: an assessment of formulae in the supine surgical patient. *Br J Anaesth* 1975; **47**: 871–5.
6. Mitchell D, Wyndham CH. Comparison of weighting formulas for calculating mean skin temperature. *J Appl Physiol* 1969; **26**: 616–22.
7. Colin J, Timbal J, Houdas Y, Boutelier C, Guieu JD. Computation of mean skin temperature from rectal skin temperature. *J Appl Physiol* 1971; **31**: 484–9.
8. Burton AC. The average temperature of the tissues of the body. *J Nutr* 1935; **9**: 264–80.
9. Sykes MK. A mixing device for expired gas. *Anaesthesia* 1968; **23**: 446–8.
10. Weir JB de V. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol* 1949; **109**: 1–9.
11. Caldwell FT, Hammel HT, Dolan F. Determination of energy balance following thermal burns by using gradient calorimetry. *Surg Forum* 1965; **16**: 486–8.
12. Carli F, Gabrielczyk M, Clark MM, Aber VR. An investigation of factors affecting postoperative rewarming of adult patients. *Anaesthesia* 1986; **41**: 363–9.
13. Stoner HB. Studies on the mechanism of shock: the impairment of thermoregulation by trauma. *Br J Exp Pathol.* 1969; **50**: 125–38.
14. Little RA, Stoner HB. Body temperature after accidental injury. *Br J Surg* 1981; **68**: 221–4.
15. Wilmore DW, Orcutt TW, Mason AD, Pruitt BA. Alterations in hypothalamic function following thermal trauma. *J Trauma* 1975; **15**: 697–703.
16. Bessey PQ, Watters JM, Aoki TT, Wilmore DW. Combined hormonal infusion simulates the metabolic response to injury. *Ann Surg* 1984; **200**: 264–80.
17. Clowes GHA Jr, George BC, Villee CA Jr, Saravis LA. Muscle proteolysis induced by a circulating peptide in patients with sepsis or trauma. *New Engl J Med* 1983; **308**: 545–52.
18. Fleck A, Colley CM, Mayers MA. Liver export proteins and trauma. *Br Med Bull* 1985; **41**: 265–73.
19. Colley CM, Fleck A, Goode AW, Muller BR, Myers MA. Early time course of the acute phase response. *J Clin Pathol* 1983; **36**: 203–7.
20. Myers MA, Fleck A, Sampson B, Colley CM, Bent J, Hall G. Early plasma protein and mineral changes after surgery: a two stage process. *J Clin Pathol.* 1984; **37**: 862–6.
21. Atkins E, Dinarello CA. Reflections of the mechanism of the biphasic febrile tolerance. In: Kluger MJ, Oppenheim JJ, Powanda MC, eds. *The Physiologic, Metabolic and Immunologic Actions of Interleukin 1 (IL-1).* New York: Alan R. Liss Inc, 1985: 97–104.
22. Moore-Ede MC, Czeisler CA, Richardson GS. Circadian timekeeping in health and disease. *New Engl J Med* 1983; **309**: 530–6.
23. Bell CF, Campbell IT, Minors DS, Waterhouse JM. Body temperature rhythms on intensive care. *Br J Anaesth* 1984; **56**: 428P.
24. Kinney JM, Roe CF. Caloric equivalent of fever: patterns of postoperative response. *Ann Surg* 1962; **156**: 610–20.
25. Barr PO, Birke G, Liljedahl SO, Plantin LO. Oxygen consumption and water loss during treatment of burns with warm dry air. *Lancet* 1968; **i**: 164–8.
26. Aulick LH, Hander EN, Wilmore DW, Mason AD, Pruitt BA. The relative significance of thermal and metabolic demands on burn hypermetabolism. *J Trauma* 1979; **19**: 559–66.
27. Carli F, Clark MM, Woollen JW. Investigation of the relationship between heat loss and nitrogen excretion in elderly patients undergoing major abdominal surgery under general anaesthetic. *Br J Anaesth* 1982; **54**: 1023–9.
28. Carli F, Itiaba K. Effect of heat conservation during and after major abdominal surgery on muscle protein breakdown in elderly patients. *Br J Anaesth* 1986; **58**: 502–7.
29. Kinney JM. *Assessment of Energy Metabolism in Health and Disease.* Columbus, Ohio: Ross Laboratories, 1980; 42–54.

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Kinetic changes in experimental colonic urinary diversion

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An experimental model of colonic urinary diversion was performed on male Wistar rats to see if faeces, urine or a faeces and urine mixture produces tumours. Cell kinetic techniques, including the crypt cell production rate, and cellular DNA measurement were used to examine the effect of urine and of faeces on the colonic mucosa. Urinary diversion into the colon significantly increased colonic crypt activity. Tumours were found at the anastomosis when urine and faeces were mixed at 4 months, and at 6 months with urine alone.

Keywords: Ureterosigmoidoscopy, colon conduit, DNA cytometry, cell kinetics

Diversion of urine from the ureters into the colon was first performed by Simon[1] in 1852 and ureterosigmoidoscopy as developed by Stiles[2] became the urinary diversion of choice. It was not until Bricker[3] developed the ileal conduit that the numbers of ureterosigmoidostomies performed declined. More recently, operations have been performed where urine only is in contact with the colonic mucosa, the colon conduit and the caecocystoplasty.

Tumours associated with ureterosigmoidostomy are well recognized, 107 having been reported in the literature, the average time to adenocarcinoma development being 26 years[4]. Recently it has been suggested that the local formation of *N*-nitrosamines from a faecal urine mix is responsible for tumour development[5] and that urine alone in contact with the colonic mucosa is safe.

Colonic adenocarcinomas have now been reported in both colon conduits[6,7] and in ileocaecocystoplasties[8] in man, suggesting that urine without faecal contamination may also be carcinogenic. The aim of this study was to determine whether urine, faeces or a urine and faecal mixture produce tumours at a urothelial colonic anastomosis. Preneoplastic changes in the colonic mucosa have been assessed with cell kinetic techniques and measurement of cellular DNA.

Method

Animals

Ninety-two male Wistar rats weighing 200 g were divided into 4 groups, with all operative procedures performed under general anaesthesia using halothane and nitrous oxide. Animals were fed a normal diet with free access to water without additional medication. The experimental groups were as follows:

Group 1 (*controls*). Non-operative controls.

Group 2 (*urothelial*). A midline incision gave access to the bladder, the dome of which was removed and implanted into the descending colon. The vesicotomy and the colotomy were closed using 6/0 Prolene (Ethicon Ltd, UK). This group acted as an operative control.

Group 3 (*colon conduit*). These rats had urine only in contact with the colon. The bladder neck was obstructed with a suture tightened around it, and the bladder anastomosed to the descending colon using 6/0 Prolene. The anastomosis site was defunctioned by a terminal colostomy brought out onto the left flank. This brought urine alone into contact with the terminal colon.

Group 4 (*vesicocolic*). In this group the bladder neck was obstructed with a suture and a vesicocolic fistula performed as in group 3 without a defunctioning colostomy. There was mixture of urine and faeces in the terminal colon of these animals mimicking a ureterosigmoidostomy.

Eight animals from each group were killed at 1, 3 and 6 months and preneoplastic changes in the colonic mucosa at the anastomosis were monitored by the crypt cell production rate (CCPR) and by colon cell DNA measurement.

Crypt cell production rate

Eight animals from each group at the three time intervals were given vincristine 1 mg kg^{-1} intraperitoneally at 8.30 a.m. on the day of death and animals killed at 30 min and then every 20 min subsequently. Weight loss in group 4 meant that the date of death was brought forward to 4 months.

Colon adjacent to the anastomosis and from the descending colon, 2 cm from the anal margin in control animals, was excised and placed in Carnoy's solution before being stained by the Feulgen technique. Under magnification the crypts were microdissected and individual crypts were separated under a cover slip. Arrested metaphases were counted from 10 crypts in each animal. The number of arrested metaphases was plotted against time and the CCPR calculated from linear regression of this line by the method of least squares and the rate expressed as cells crypt^{-1} h^{-1}.

Cellular DNA measurement

Colonic mucosa in the descending colon of controls and adjacent to the anastomosis in groups 2, 3 and 4 was brushed to remove cells from the upper portions of the colonic crypts. The cells were collected in Hank's solution and cytopreparations prepared by centrifugation. These were stained by the Feulgen technique which binds to the DNA stoichiometrically and the DNA content of 100 epithelial cells was determined by microdensitometry. The percentage of cells with more than the diploid amount of DNA was called the proliferative index (PI). The CCPRs were compared using a paired *t* test. The PIs were compared by the Mann–Whitney *U* test.

Results

Crypt cell production rate

At 1 month, the CCPR in control animals was 4·9 cells crypt^{-1} h^{-1} and this value remained constant throughout the experiment (*Table 1*). The CCPR of the animals with a urothelial implant was consistently but insignificantly higher than the control animals at all time intervals studied (*Table 1*). At 1 month the CCPR in animals with a colonic conduit was 27·6 cells crypt^{-1} h^{-1} and in those with a vesicocolic anastomosis 23·5 cells crypt^{-1} h^{-1}, both of which were substantially higher than controls ($P<0{\cdot}005$). These high CCPR values were maintained in both of the urinary diversion groups throughout the experiment.

Table 1 *The CCPRs (cells crypt^{-1} h^{-1}) of the four groups of animals*

	Time after operation (months)		
	1	3	6
Control	4·9	3·4	2·4
Urothelial implant	7·4	5·9	9·5
Conduit	27·6	21·1	34·3
Vesicocolic	23·5	22·9	20·9*

* Value at 4 months

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Table 2 *Mean proliferative index ± s.e.m. of the four groups of animals*

	Time after operation (months)		
Group	1	3	6
Control	1·7 ± 0·5	1·3 ± 0·6	1·7 ± 0·3
Urothelial implant	0·9 ± 0·3	0·8 ± 0·5	6·4 ± 0·9
Colon conduit	4·5 ± 0·6	8·4 ± 2·1	7·6 ± 1·0
Vesicocolic anastomosis	4·9 ± 0·3	7·0 ± 1·8	11·8 ± 1·1*

* Value at 4 months

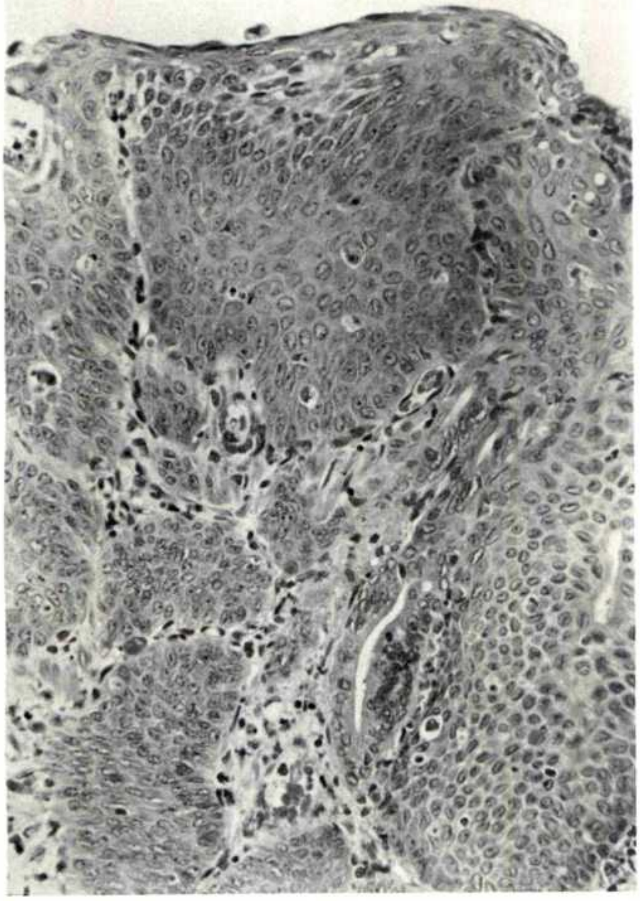

Figure 1 *A 6-month urothelial implant showing proliferating urothelium with areas of squamous metaplasia (haematoxylin and eosin × 250)*

Cellular DNA measurement

In control animals the mean PI was 1·7 and was similar at 3 and 6 months (*Table 2*). There was no significant difference between the urothelial implant group and the control groups at 1 and 3 months but by 6 months there was a significant increase to 6·4 ($P < 0·001$) in the urothelial implant group compared with the non-operative controls. At 1 month the mean PI of the colon conduit group (4·5) and that of the vesicocolic group (4·9) were significantly greater than the values obtained at 1 month for both of the control groups. These high values were maintained throughout the experiment.

Macroscopic appearance

There were no macroscopic changes in the control rats or in the urothelial group until 6 months. At 6 months, the urothelial group formed diverticula with small tumours (0·1 cm) at the suture line. The colonic conduit group also had small tumours at the anastomosis at 6 months. The vesicocolic group at 3 months had developed small tumours, one of which was 0·2 cm across. At 4 months, all the rats in this group had developed tumours that filled the lumen of the bowel.

Microscopic appearance

The colonic mucosa of the non-operative and urothelial implant groups remained normal throughout. In all the urothelial implant animals at 6 months there was hyperplasia of the urothelium (*Figure 1*) with keratinization in two rats and glandular and squamous metaplasia in three others.

The colonic mucosa of the colon conduits showed lengthening and bunching of the crypts as early as 1 month. The urothelium at the anastomosis at 6 months showed marked proliferation and in some places both squamous metaplasia with some keratinization and glandular proliferation were present (*Figure 2*). The vesicocolic group also showed similar colonic mucosal changes and by 3 months squamous metaplasia of the urothelium with some glandular changes was seen (*Figure 3*).

Discussion

Various theories have been suggested to explain the malignant change in the colon following ureterosigmoidostomy, including mechanical effects[9], age of anastomosis[10], and the irritative effect of urine[11], or its electrolyte environment[12]. More recently the mixture of urine and faeces in experimental animals[13] and man[5] has been shown to produce *N*-nitrosamines which are known carcinogens[14]. These theories assume that the tumours produced are colonic in origin. Chiarelli and Sandei have suggested that they are urothelial in origin, developing from glandular metaplasia of the urothelium[15].

This investigation has demonstrated that diversion of urine into the colon leads to an increase in proliferative activity in the epithelium whether or not faeces are present. The CCPR, which is the most sensitive technique available for assessing changes in crypt cell kinetics[16] showed a fourfold increase at 1 month compared with controls in animals with colon conduits and with vesicocolic anastomoses. These differences in crypt proliferation were maintained to the end of the experiments at 6 months. A small but consistent increase in CCPR was also seen in the urothelial group, possibly due to anastomotic healing or the irritative effect due to presence of a 'foreign' tissue. A similar rise in CCPR has been observed prior to the development of colonic cancer in rats treated with azoxymethane[17]. These results suggest that urine is responsible for the proliferative changes as there was no difference in CCPR between the colon conduit and vesicocolic groups.

The second kinetic technique confirms the CCPR results. By brushing the surface mucosa with a cytological brush, cells from the upper portion of the crypt are released where active cell division is not normally seen[18]. The DNA content of cells varies

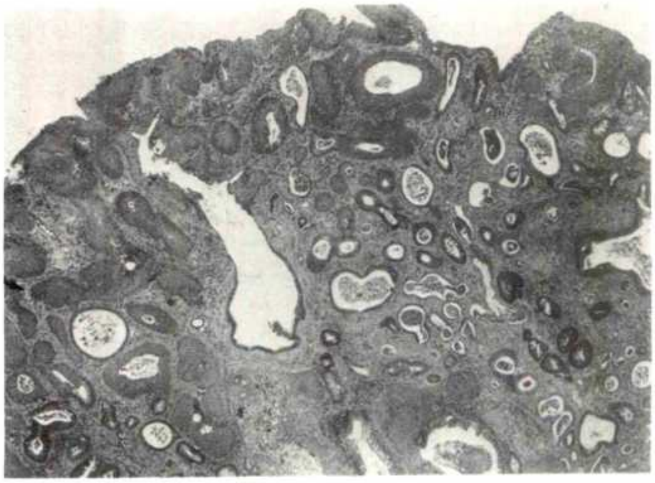

Figure 2 *Anastomotic site of a 6-month colonic conduit showing marked proliferation of urothelium with underlying and adjacent proliferation of glandular elements (haematoxylin and eosin × 40)*

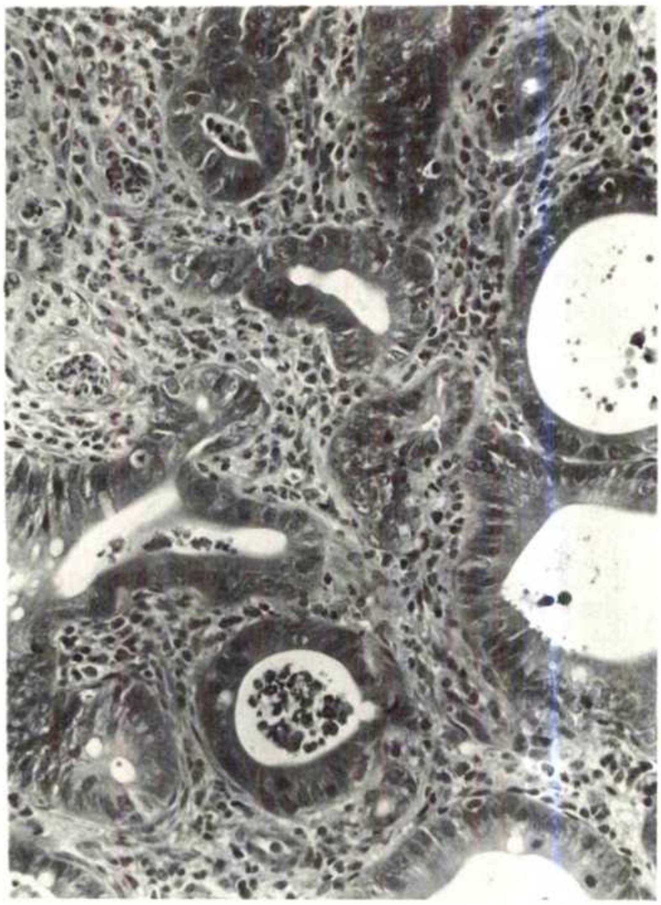

Figure 3 *Anastomotic site of a 3-month vesicocolic anastomosis showing proliferating glandular elements with architectural distortion and marked cytological atypia (haematoxylin and eosin ×250)*

with the phase of the cell cycle; those in the S, G_2 and mitotic phases will contain a hyperdiploid amount of DNA. The hyperdiploid or PI will therefore reflect cell proliferation in the upper part of the crypt. The expected low PI was seen in the control and urothelial implant groups at 1 and 3 months. In both the vesicocolic and colon conduit animals there was a significant rise in PI at 1 month compared with that in the control animals and there was a further rise at 6 months. A similar shift of proliferating cells into the upper portion of the crypt has been described in animal models of colonic carcinogenesis and in humans who are at high risk of developing colonic tumours[18,19].

All the animals in the vesicocolic group developed tumours by 4 months. These were obvious macroscopically and caused deaths in two animals. Tumours also formed in the rectal bladder group but were not obvious until 6 months. This suggests that although urine alone initiates the kinetic changes associated with carcinogenesis, faeces or a urine faeces mixture does play a part in promoting the carcinogenic process. A mixture of urine and faeces has been shown in experimental animals to produce *N*-nitrosamines which are known to be carcinogenic[14]. At the site of anastomosis there are marked histological changes. There is extensive proliferation of the urothelium with adjacent and even underlying proliferation of glandular elements, which in some areas have all the histological criteria of neoplasia. It is difficult to define whether these glandular elements arise from metaplastic urothelium or from colonic mucosa.

The kinetic data produced correlate with the histological structure of the mucosa at the anastomosis site of the four study groups. Throughout the experimental period no change was seen in the colon of animals in the two control groups whereas there were obvious histological changes in the colon of animals in the other groups. The crypts were grossly elongated, as would be expected from the increase in CCPR, but they also developed a villous structure. These effects were most marked at the anastomosis probably because this is where the urine concentration was highest, but they were still seen distal to this site.

Increase in crypt proliferation with the development of tumours when urine alone is in contact with colonic mucosa suggests that patients undergoing caecocystoplasty or having a colon conduit are at high risk of neoplastic changes. Evidence from observation after ureterosigmoidostomy suggests that these tumours may take up to 30 years to develop[4] and therefore these patients ought to be followed for life.

References

1. Simon J. Ectopia vesicae. *Lancet* 1852; 568–70.
2. Stiles H. Epispadias in female and its surgical treatment. *Surg, Gynecol Obstet* 1911; **13**: 127–40.
3. Bricker EM. Bladder substitution after pelvic evisceration. *Surg Clin North Am* 1950; **30**: 1511–21.
4. Stewart M, Macrae FA, Williams CB. Neoplasia and ureterosigmoidostomy: a colonoscopy survey. *Br J Surg* 1982; **69**: 414–16.
5. Stewart M, Hill MH, Pugh RCB, Williams JP. The role of N-nitrosamine in carcinogenesis at the ureterocolic anastomosis. *Br J Urol* 1981; **53**: 115–18.
6. Chiang MS, Minton JP, Clausen K, Chalworthy HW, Wise HA. Carcinoma in a colon conduit urinary diversion. *J Urol* 1982; **127**: 1185–7.
7. Wilson JWL, Morales A. Development of adenocarcinoma in transverse colon conduit. *Urology* 1892; **20**: 182–3.
8. Kirby RS, Lloyd-Davies RW. Adenocarcinoma occurring within a caecocystoplasty. *Br J Urol* 1985; **57**: 357–8.
9. Tank ES, Karsch DN, Lapides J. Adenocarcinoma of the colon associated with ureterosigmoidostomy: a report of a case. *Dis Colon Rectum* 1973; **16**: 300–4.
10. Carswell JJ, Skeel DA, Witherington R, Otken LB. Neoplasia at the site of ureterosigmoidostomy. *J Urol* 1976; **115**: 750–2.
11. Urdaneta LF, Duffield D, Creevy CD, Aust JB. Late development of primary carcinoma of the colon following ureterosigmoidostomy: a report of three cases and literature review. *Ann Surg* 1966; **164**: 503–13.
12. Harguindey SS, Kolbeck RC, Bransome ED. Ureterosigmoidostomy and cancer, new observations. *Ann Intern Med* 1973; **83**: 833.
13. Stewart M. Urinary diversion and cancer. MS Thesis, University of London 1984: 150–9.
14. Habs M, Schmahl D. Diet and cancer. *J Cancer Res Clin Oncol* 1980; **96**: 1–10.
15. Chiarelli SM, Sandei F. Polyps at the site of ureterosigmoidostomy. *Tumori* 1984; **70**: 209–15.
16. Wright NA. Cell proliferation in the normal gastrointestinal tract: implications for proliferative response. In: Sunter JP, Watson AAJ, eds. *Cell Proliferation in the Gastrointestinal Tract*. Tunbridge Wells: Pitman Medical, 1984: 8.
17. Matthews J, Cooke T. Changes in crypt cell DNA control content during experimental colonic carcinogenesis. *Br J Cancer* 1986; **53**: 787–91.
18. Sunter JP. Cell proliferation in gastrointestinal carcinogenesis. *Scand J Gastroenterol* 1984; **19** (Suppl 104): 45–55.
19. Lipkin M. The identification of high risk populations. *Scand J Gastroenterol* 1984; **19** (Suppl 104): 91–7.

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Exfoliated cells and in vitro growth in colorectal cancer

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Cells exfoliated from colorectal cancers may only be implicated in local recurrence if they are proven to be viable and capable of growth. Thirty patients with primary colorectal cancer were studied. Cells were obtained from primary tumour, uninvolved mucosa, mesorectum, lumen of the bowel, luminal mucus, serosal surface of the bowel and from washings of the tumour bed after dissection. Colonies grew in vitro *in monolayer culture from 21/30 primary tumours; 11/41 mesorectum specimens; 11/27 luminal washings; 14/29 luminal mucus specimens; 1/27 serosal surface washings and 3/13 post-dissection washes. Colonies stained positively for the epithelial markers cytokeratin and desmosomes and also for carcinoembryonic antigen. Cells capable of* in vitro *growth are present in these various sites and, if spilled at operation, may well be implicated as one of the factors leading to local recurrence.*

Keywords: Colorectal cancer, local recurrence, exfoliated cells, *in vitro* growth

Colorectal cancer is a common disease in Western society and local recurrence after conceivably curative resection is a major problem. Low rectal carcinomas carry the highest rates of local recurrence, with most series reporting 10–20 per cent[1], although figures vary from 3·7 per cent[2], to 31 per cent[3] and more. Local recurrence is not, however, confined to tumours of the rectum. A recently reported multicentre study reported approximately 12 per cent local recurrence for the entire colon except for the splenic flexure where the figure was 19 per cent[4].

Malignant cells giving rise to local recurrence may, in theory, be derived from several sources. Prominent among these are the bowel lumen[5], serosal surface[6] and from deposits within the mesorectum[7]. However, incomplete resection of the primary must rank as a major consideration[8,9]. In addition, the possibility of *de novo* suture-line malignancy where the mucosa has undergone a field change may be a factor[10].

In the last decade, controversy has again been raised with regard to whether cells exfoliated into the lumen of the bowel are viable. Rosenberg *et al.*[11] reported no viable cells in luminal washings whereas Umpleby *et al.*[5] demonstrated viable cells in 70 per cent of resected specimens as assessed by trypan blue exclusion. However, it is necessary to prove a potential for growth if exfoliated cells are to be regarded as contributing to local recurrence.

The aims of this study were to isolate exfoliated colorectal cancer cells and to assess their potential for growth in an *in vitro* culture system.

Methods

Thirty patients with colorectal cancer were studied; 17 had tumours classified as rectal, i.e. with the lower edge 15 cm or less from the anal verge. At laparotomy, samples were obtained as follows:

Washings. When the abdomen was opened, the serosal surface of the tumour was washed with 50 ml of saline from a syringe. After gentle agitation, the saline was aspirated. A lavage of the tumour bed following resection and anastomosis was performed with a further 50 ml of saline. The lumen of the operative specimen was lavaged from the distal end with 50 ml of saline, without squeezing the tumour itself, and aspirated. In some low anterior resections, a saline wash of the rectal stump was performed through a proctoscope after cross-clamping but before division of the bowel.

Tissue specimens. In the rectal tumours, after resection of the specimen but before the occluding clamps were removed, a block of tissue 3 cm × 3 cm × 2 cm was taken from the posterior aspect of the mesorectum at the level of the tumour in all cases. Where possible a similar sized block was taken 5 cm above and/or 5 cm below the tumour. Although macroscopic tumour was present in some of the blocks of mesorectum, in no case did the block extend down to the bowel wall or primary tumour. Clamps were removed and, after performing the luminal wash, the specimen was opened. A smear of luminal mucus was taken from near to the tumour with a wooden spatula, ensuring that the tumour itself was not touched. The specimen was then washed under the tap to remove any remaining faecal debris, mucus and blood. A 1 cm block was taken from the rolled edge of the tumour. A 2 cm × 2 cm area of uninvolved mucosa at the proximal resection margin was removed by dissecting in the submucosal layer.

Transport of specimens

All 50 ml saline washings were transported with 10 per cent newborn calf serum (Gibco), heparin 1000 units, piperacillin 80 mg/ml (Lederle), amphotericin 100 mg/ml (Squibb) and nystatin 100 units/ml. (Squibb). Tissue blocks and mucus were transported in Hank's balanced salt solution (Hank's BSS) (Gibco) with piperacillin, amphotericin and nystatin as above. All specimens were transported at room temperature.

Preparation of cell suspensions

Washings and the mucus specimens were spun down and washed twice in Dulbecco's modified Eagle's medium (DMEM) (Gibco) with Hepes buffer 25 mM and added antibiotics as above. Tissue specimens were chopped finely with scalpel blades and then enzymatically disaggregated using a cocktail of protease 0·5 mg/ml (Sigma No. P5647) and deoxyribonuclease 0·005 mg/ml (Sigma No. D4638) in Hank's BSS and antibiotics. Incubation was performed at room temperature on a rolling mixer (Spiramix) for 45–60 min. Tumour and mucosa specimens were washed twice in Hank's BSS before disaggregation, but mesorectum specimens were disagggregated in the original transport solution so that any cells leaking from blood vessels or lymphatics would not be lost. After disaggregation, the resulting suspension was filtered through a fine plastic strainer to remove gross particles and washed twice in DMEM with Hepes buffer and antibiotics. Finally, all cell preparations were taken up in McCoy's 5A (MCA) (Gibco) with 10 per cent fetal calf serum, and piperacillin, amphotericin and nystatin as above to a volume of 6–10 ml.

Viability counts

These were performed on the final cell suspensions using acridine orange/ethidium bromide supravital staining[12]. Nuclei of live cells fluoresce green and the nuclei of dead cells fluoresce red in blue light using dark ground illumination.

Cell cultures

A cell culture for each specimen was set up in 25 cm^2 culture flasks (Nunc). For each specimen, 4 ml of cell suspension in MCA, serum, antibiotics and 1 ml of DMEM containing 10^5 mouse fibroblasts (C3H10T1/2)[13] was added to each flask. These were incubated at 37°C in 5 per cent CO_2 in humidified air and examined daily. Medium was changed at 24 h and thereafter every 3 or 4 days. At medium changes,

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culture supernatants were taken and stored at −20°C for carcinoembryonic antigen (CEA) assay. The fibroblast population was kept in check by regular differential trypsinization using 0·5 ml trypsin/EDTA solution (Gibco) in 5 ml of Dulbecco's phosphate-buffered saline (PBS) (Gibco) in each flask. For certain specimens, culture slide flasks (Nunc) or four chamber slides (Miles Scientific) were set up using 3·5 ml cell suspension and 0·75 ml fibroblast suspension in the culture slide flasks, and the same volume shared between each of the chambers in the four chamber slides. These enabled direct staining of colonies while preserving the colony morphology. No trypsinization was attempted in these systems but after 5–10 days, when colonies had appeared, the slides were washed with PBS, air dried and stored desiccated at −20°C. This was to avoid loss of colonies through regression, although as a result the colonies in these systems tended to be smaller than those in the 25 cm² flasks.

Staining

Mouse monoclonal antibodies were used to stain for CEA (Parlam 4) and the epithelial markers cytokeratin (Cam 5·2 Beckton Dickinson) and desmosomes (F511). Staining was performed using an alkaline phosphatase-antialkaline phosphatase (APAAP) Universal kit (Dako). Counterstaining was performed with Meyer's Haemalum and preparations were mounted using glycerol (Dako). This system gives a pink stain when positive. A negative control stain using the APAAP but no primary antibody was performed with each specimen to check that endogenous alkaline phosphatase activity or non-specific link antibody binding were not giving false positive results. Some colonies were stained with anti leu-3 (Beckton Dickinson) to see if they contained macrophages.

CEA assays

These were performed on culture supernatants using an immunoabsorbent assay for CEA (Abbott).

Results

Cultures

Thirty patients were studied (fourteen men, sixteen women) with a median age 67·5 years (range 30–89). There were 5 right colon tumours, 3 transverse, 5 left sided (4 sigmoid) and 17 rectal tumours. Nine rectal tumours were within 6 cm of the anal verge and eight between 7–15 cm from the anal verge. *Table 1* shows the total number of samples for each specimen and the number growing colonies. In the tumour, luminal wash and mucus specimens approximately 10–20 colonies grew in the positive cultures. For rectal wash and mesorectum specimens, 2–5 grew and in the normal mucosa an isolated colony grew in each of the five positive samples. All colonies had a similar morphology with flat spreading and heaped up areas. Most colonies regressed spontaneously in 10–14 days. However, in three patients growth of certain colonies derived from disaggregated tumours continued for 1 month and in one patient growth continued for 2 months. These colonies could be removed by using the protease/deoxyribonuclease cocktail in DMEM at the concentrations referred to earlier and passaged into other flasks.

Bacterial and fungal infections, not surprisingly, were a problem and losses of cultures through infection (*Table 1*) occurred either early (in the first 5 days, probably through infection carried over from the original preparations) or late (almost certainly due to infection introduced during handling of the culture). Early losses almost always occurred before growth of colonies but in some cases late infection resulted in loss of established colonies.

There was no association between Dukes' staging and growth in culture for most specimens (*Table 2*). Notably, of a total of 11 mesorectum specimens growing colonies, 9 were from C tumours, one was a B tumour and one an A tumour. However, in the case of the A tumour, the resected specimen was opened by the surgeon in theatre so that contamination with luminal cells could not be definitely excluded. There was no association between histological grading of the tumours and growth in culture (*Table 3*). Colonies were grown from both well and poorly differentiated tumours.

Table 2 *Dukes' staging and growth*

	Number growing/ total number		
	A	B	C
Primary tumour	1/1	12/15	8/14
Proximal mucosa	0/1	3/15	2/13
Luminal washings	1/1	5/12	5/14
Luminal mucus	1/1	6/15	7/13
Rectal stump washings	0/0	2/4	0/2
Mesorectum at tumour level	1/1	0/5	4/11
Mesorectum 5 cm above tumour	0/1	0/4	4/10
Mesorectum 5 cm below tumour	0/0	1/3	1/6
Serosal surface washings	0/1	1/14	0/12
Post-dissection lavage tumour bed	0/0	2/7	1/6

Table 3 *Histological differentiation and growth*

	Number growing/ total number		
	Well	Moderate	Poor
Primary tumour	4/4	12/18	5/8
Proximal mucosa	1/4	2/17	2/8
Luminal washings	0/3	9/17	2/7
Luminal mucus	1/4	8/18	5/7
Rectal stump washings	0/1	1/3	1/2
Mesorectum at tumour level	0/1	3/12	2/4
Mesorectum 5 cm above tumour	0/1	1/10	3/4
Mesorectum 5 cm below tumour	0/0	1/7	1/2
Serosal surface washings	0/4	1/17	0/6
Post-dissection lavage tumour bed	0/1	1/8	2/4

Table 1 *Number of samples growing colonies and losses through infection*

Origins of specimens	Total number	Number growing colonies	Percentage growth	Infections	
				Early	Late
Primary tumour	30	21	70	5	7
Proximal mucosa	29	5	17	4	2
Luminal washings	27	11	41	6	5
Luminal mucus	29	14	48	4	5
Rectal stump washings	6	2	33	2	0
Mesorectum at tumour level	17	5	29	2	4
Mesorectum 5 cm above tumour	15	4	27	1	3
Mesorectum 5 cm below tumour	9	2	22	0	2
Serosal surface washings	27	1	4	3	4
Post-dissection lavage tumour bed	13	3	23	2	4

Table 4 *Production of CEA by cultured cells*

Tumour	Period in culture		CEA values (ng/ml)	
	From day	To day	Initial	Final
1	29	38	2·5	8·0
2	36	47	7·0	28·0
3	15	23	41·5	48·5
4	11	18	24·0	43·0

Viability counts

Counts of viable cells varied considerably between the samples in any given group of specimens. However, there was no significant difference in the number of cells plated between those samples which grew colonies and those which did not. Accurate cell counts were difficult since many cells were in clumps and so counts were only estimates. However, cells in clumps often had the highest viability on supravital staining and many clumps of viable cells were seen particularly in the mucus specimens.

Colony staining

All colonies grown in culture slides or four chamber slides were morphologically identical to each other and identical to the colonies grown in the main culture flasks. All the colonies stained positively for CEA, cytokeratin and desmosomes. Colonies stained negatively with anti-leu3, indicating that these cells were not macrophages. All control stains were negative, indicating that neither endogenous alkaline phosphatase activity in the colonic epithelium nor non-specific link antibody binding was giving false positive staining.

CEA assays

CEA levels in cultures of luminal washings, luminal mucus and tumours were initially high, but decreased after the first two or three changes of medium. CEA is present in the lumen of the bowel in large quantities, explaining this phenomenon[14]. In those tumours ($n=4$) where growth progressed beyond 10–14 days, a rise in CEA in the supernatant was seen (*Table 4*) indicating production of CEA by the cultured cells.

Discussion

Cells exfoliated from cancers have, in the past, been considered capable of implanting and giving rise to local recurrence or metastatic deposits[15]. Hence most surgeons utilized some form of antiseptic/antitumour agent to wash out the lumen of the bowel at the site of the anastomosis in order to remove exfoliated malignant cells and hopefully reduce local recurrence[16]. In addition, specific case reports have been cited of adenocarcinomas growing on haemorrhoidectomy wounds and fissures in the presence of an occult primary[17,18], giving further weight to the hypothesis that exfoliated malignant cells were capable of implantation and growth. In the last decade, however, controversy has arisen as to whether exfoliated cells are indeed viable. Rosenberg *et al.*[11] reported no viable cells as assessed by trypan blue exclusion. However, Umpleby *et al.*[5] showed that 70 per cent of patients with colorectal cancer had viable cells exfoliated into the lumen of the bowel as assessed by trypan blue exclusion and hydrolysis of fluorescein diacetate. Umpleby and Williamson[19] reported a questionnaire sent to surgeons in the southwest of England. Two-thirds routinely used intraluminal cytotoxic agents, the most popular being chlorhexidine–cetrimide, povidone–iodine, mercuric perchloride and water. In low anterior resections, lavage was performed either from below before division of the bowel or from above after division. In more proximal resections the bowel ends were swabbed with the agent after division. One-third of the 72 surgeons replying no longer took any special precautions to prevent implantion of cells from the lumen of the bowel before performing an anastomosis.

To implicate cells in local recurrence they must be shown to have potential for growth. Fermor *et al.*[20] reported tail vein injections of luminal exfoliated cells from 17 patients into immune deprived mice. In six cases, this resulted in lung tumours histologically distinct from the spontaneous pulmonary tumours known to develop in these animals. Immune deprived animals would have been difficult to handle in view of the contaminated nature of the samples in this study and would have been very expensive due to the number of samples taken.

However, if exfoliated cells have malignant potential, as well as producing distant metastases in these animal models they should also demonstrate the ability for *in vitro* growth. This provides a much more easily handled system for demonstrating growth potential and, if cells will grow *in vitro*, it is very reasonable to suppose that they will also grow *in vivo*. From the results of the present study it is apparent that cells with potential for *in vitro* growth have been demonstrated in the lumen of the bowel, in the mesorectum, and occasionally from the serosal surface. In addition they may be present in the tumour bed after dissection.

The epithelial nature of these cells has been proven by their staining for both cytokeratin and desmosomes, and their colonic origin by their staining for CEA. Their malignant nature is strongly inferred by the readiness with which they grow in monolayer culture. Twenty-one of thirty primary tumours grew 10–20 colonies but only five of twenty-nine uninvolved mucosa specimens grew a single colony each. Growth of primary tumours in this culture system is common and well documented[21,13] but no reports of normal mucosa growing in this relatively unsophisticated system exist[22]. It was felt that the isolated colonies growing from the uninvolved mucosa specimens were mostly likely to have originated from contamination by malignant cells which had been exfoliated into the lumen and had been carried proximally by the lavage.

What is the role of these cells in the development of local recurrence? Much discussion has centred around free luminal cells implanting onto a colonic suture-line and hence leading to the relatively uncommon suture-line recurrence[16]. Local recurrence also arises within the bowel wall or within the tissues adjacent to the bowel[23]. Inadequate surgical excision of the primary tumour, lymphatic drainage and the mesorectum are clearly of importance in this regard[7,8], but a further contribution may be spillage and subsequent seeding of free cells from the lumen of the bowel or from the mesorectum. The high rates of local recurence after low anastomosis (which is being performed more commonly following the advent of the circular staplers) may well be explained partly by failure to excise the entire mesorectum and partly by failure to wash from the lumen of the bowel cells which would otherwise be carried proximally during introduction of the stapler from below. Trauma to any tissue makes it a more favourable environment for metastases to develop[24,25] and surgical trauma enhances the 'soil-effect' in bowel anastomoses and laparotomy wounds in experimental animals. Exfoliated cells that are spilled onto the area of dissection encounter an environment made more favourable for growth by the trauma of surgery.

It is apparent from the results of this study that care should be taken to avoid spillage of cells from the lumen of the bowel. It is clearly prudent to clean the bowel ends with a tumoricidal agent before anastomosis and to wash out the tumour bed after resection and anastomosis. The efficacy of a number of agents has recently been reviewed and recommendations for choice of agents made[19]. The rectal stump should be washed out after cross-clamping and before division in low anterior resections. Equally, it is important to avoid tearing into or dividing the mesorectum and careful total excision by sharp dissection should probably be practised[2,7].

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References

1. Phillips RKS, Hittinger R, Blesovsky L, Fry JS, Fielding LP. Local recurrence following 'curative' surgery for large bowel cancer: II. The rectum and rectosigmoid. *Br J Surg* 1984; **71**: 17–20.
2. Heald RJ, Ryall RDH. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986; **i**: 1479–82.
3. Hurst PA, Prout WG, Kelly JM, Bannister JJ, Walker RT. Local recurrence after low anterior resection using the staple gun. *Br J Surg* 1982; **69**: 275–6.
4. Phillips RKS, Hittinger R, Blesovsky L, Fry JS, Fielding LP. Local recurrence following 'curative' surgery for large bowel cancer: I. The overall picture. *Br J Surg* 1984; **71**: 12–6.
5. Umpleby HC, Fermor B, Symes MO, Williamson RCN. Viability of exfoliated colorectal carcinoma cells. *Br J Surg* 1984; **71**: 659–63.
6. Quan SHQ. Cul-de-sac smears for cancer cells. *Surgery* 1959; **45**: 258–63.
7. Heald RJ, Husband EM, Ryall RDH. The mesorectum in rectal cancer surgery—the clue to pelvic recurrence? *Br J Surg* 1982; **69**: 613–16.
8. Enker WE, Laffer UT, Block GE. Enhanced survival of patients with colon and rectal cancer is based upon wide anatomic resection. *Ann Surg* 1979; **190**: 350–60.
9. Goligher JC, Dukes CE, Bussey HJR. Local recurrences after sphincter-saving excisions for carcinoma of the rectum and rectosigmoid. *Br J Surg* 1951; **39**: 199–211.
10. Williamson RCN, Davies PW, Bristol JB, Wells M. Intestinal adaptation and experimental carcinogenesis after partial colectomy. *Gut* 1982; **23**: 316–25.
11. Rosenberg IL, Russell CW, Giles GR. Cell viability studies on the exfoliated colonic cancer cell. *Br J Surg* 1978; **65**: 188–90.
12. Parks DR, Bryan VM, Oi VT, Herzenberg LA. Antigen-specific identification and cloning of hybridomas with a fluorescence-activated cell sorter. *Proc Natl Acad Sci USA* 1979; **76**: 1962–6.
13. Brattain MG, Brattain DE, Sarrif AM, McRae LJ, Fine WD, Hawkins JG. Enhancement of growth of human colon tumour cell lines by feeder layers of murine fibroblasts. *J Natl Cancer Inst* 1982; **69**: 767–71.
14. Poleski MH, Blattner WA, Chait M *et al.* CEA in colonic lavage of individuals at high risk of large bowel cancer. *Gastroenterology* 1978; **74**: 1140.
15. Keynes WM. Implantation from the bowel lumen in cancer of the large intestine. *Ann Surg* 1961; **153**: 357–64.
16. Southwick HW, Harridge WH, Cole WH. Recurrence at the suture line following resection for carcinoma of the colon. *Am J Surg* 1962; **103**: 86–9.
17. Le Quesne LP, Thompson AD. Implantation recurrence of carcinoma of rectum and colon. *N Engl J Med* 1958; **258**: 578–82.
18. Killingback M, Wilson E, Hughes ESR. Anal metastases from carcinoma of the rectum and colon. *Aust NZ J Surg* 1965; **34**: 178–87.
19. Umpleby HC, Williamson RCN. The efficacy of agents employed to prevent anastomotic recurrence in colorectal carcinoma. *Ann R Coll Surg Engl* 1984; **66**: 192–4.
20. Fermor B, Umpleby HC, Lever JV, Symes MO, Williamson RCN. Proliferative and metastatic potential of exfoliated colorectal cancer cells. *J Natl Cancer Inst* 1986; **76**: 347–9.
21. Kirkland SC, Bailey IG. Establishment and characterisation of six human colorectal adenocarcinoma cell lines. *Br J Cancer* 1986; **53**: 779–85.
22. Danes BS, Sutanto E. Epithelial line from normal human colon mucosa. *J Natl Cancer Inst* 1982; **69**: 1271–3.
23. Tyndal EC, Dockerty MB, Waugh JM. Pelvic recurrence of carcinoma of the rectum. *Surg Gynecol Obstet* 1964; **118**: 47–51.
24. Jones FS, Rous P. On the cause of the localisation of secondary tumours at points of injury. *J. Exp Med* 1914; **20**: 404–12.
25. Alexander JW, Altemeier WA. Susceptibility of injured tissues to haematogenous metastases: an experimental study. *Ann Surg* 1964; **159**: 933–44.

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Non-invasive endoscopic technique to assess gastrointestinal perfusion

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Changes in mucosal blood flow may occur in many gastrointestinal disorders, but assessment is impossible without a non-invasive in vivo *technique. We have compared endoscopic laser Doppler (LD) with oxygen electrode (OE) measurements in a dog isolated colon preparation, using variable perfusion measured with an electromagnetic flow probe. At maximum flow, LD measurements were made at three sites to compare mucosal with serosal readings. Flow rate was varied (1–38 ml/min) and measurements of microcirculatory flux obtained using LD, and of oxygen tension using a serosal OE. A progressive trend towards increasing flux was demonstrated from caecum to rectum—serosa: 46·8 ± 18·7 V (caecum), 52·6 ± 17·9 V (mid-colon) and 61·3 ± 17·6 V (rectum). A parallel trend was observed in mucosal values: 41·1 ± 18·2 V (caecum), 45·7 ± 15·2 V (mid-colon) and 54·1 ± 15·1 V (rectum). At all sites, serosal and mucosal values were not significantly different (Student's* t *test). LD serosal values correlated significantly with EM flow* ($r = 0{\cdot}544$, $0{\cdot}01 > P > 0{\cdot}001$)*. A similar linear correlation was found between OE and EM flow* ($r = 0{\cdot}65$, $P < 0{\cdot}001$)*. Oxygen tension measurements varied as expected with microcirculatory flux* ($r = 0{\cdot}441$, $0{\cdot}02 > P > 0{\cdot}01$)*. Endoscopic LD assessment of colonic microcirculation accurately reflects changes in blood flow.*

Keywords: Colonic blood flow, oximetry, laser Doppler

Most of our knowledge about microcirculation has been gained indirectly from experimental results extrapolated to the human, or from *in vitro* studies on micro-anatomy. A new instrument, laser Doppler, uses a fibreoptic probe small enough to pass along the biopsy channel of a flexible endoscope, perhaps permitting *in vivo* studies of gastrointestinal mucosal perfusion in patients.

The laser Doppler technique of measuring blood flow was developed by two groups, Watkins and Holloway[1] in America and Nilsson, Tenland and Oberg[2] in Sweden. Briefly, according to the Doppler principle, any radiation which is reflected from a moving object undergoes a shift in frequency, and therefore also in wavelength. In the case of light, this is shifted towards the red end of the spectrum. In the laser Doppler instrument, coherent light is generated by a helium–neon source at 632·8 nm. This is directed at the tissue under study via a flexible optical fibre. All moving cells (principally red blood cells) within this volume of tissue will be struck by the light and will reflect some of it; the reflected light will be Doppler shifted and form an interference pattern with unshifted light reflected from stationary cells. The reflected light is collected in two more optical fibres, and returned to the instrument where it is then analysed mathematically to give a measure of the amount of cellular movement under the probe which is termed the flux. Flux is thus defined as the number of cells moving in the measured volume multiplied by the mean velocity of those cells. Since the erythrocytes in the capillaries are moving in many different directions, the instrument does not give a direct measure of tissue blood flow, and the flux is registered arbitrarily as the voltage output of the instrument (V).

We have evaluated this technique in the dog colon and compared it with an existing experimental method, oximetry.

Methods and results

In vitro *reproducibility*

Laser Doppler readings, at 5-s intervals, were made with the standard probe suspended in 20 ml of milk (a uniform emulsion) at 10°C. The Pf2 (Perimed, Sweden) instrument was used, with the probe unheated and a gain of 1.

With a frequency limit (bandwidth) of 4–20 kHz, mean flux after 44 readings was 37·6 ± 0·49 V (± s.d.); coefficient of variation for this bandwidth was 1·25 per cent. When the experiment was repeated using a bandwidth of 12–20 kHz, mean flux rose to 66·6 ± 0·72 V; the coefficient of variation at this level was 1·1 per cent.

In vivo *reproducibility*

Six beagle dogs (average weight 14 kg) were given 2·5 g sodium picosulphate, then a fluid diet for 24 h. They were premedicated with barbiturate, then anaesthesia was induced with sodium pentobarbitone (25 mg/kg), an endotracheal tube passed, and the animals maintained on nitrous oxide and oxygen. The colon was exposed by a midline laparotomy and, starting at the pelvic brim, three silk sutures placed 5 cm apart were used to mark sites along the colon. Six readings were then made from each site using the standard LD probe held against the serosa by hand.

The results are shown in *Table 1*. The mean coefficient of variation is 16·9 per cent.

Serosal compared with mucosal readings

A caecostomy was created to pass a large Foley catheter (24 french) through which orthograde lavage of the colon was performed using warmed normal saline, until the effluent ran clear. The endoscopic probe was passed via the biopsy channel of a flexible endoscope (KeyMed), itself passed per rectum. At the same three sites, six further readings were recorded using the endoscopic probe held against the mucosa.

Mean serosal flux in the lower colon was 60·8 ± 5·1 V which was not significantly different from the mean mucosal flux of 54·0 ± 9·1 V (Student's *t* test). In mid-colon, mean serosal flux of 48·0 ± 15·3 V was similar to mean mucosal flux, 47·0 ± 8·4 V. This was also found in the upper colon—serosal flux 47·0 ± 15·1 V, mucosal flux 41·0 ± 13·9 V.

Variation of laser Doppler readings with arterial inflow

That part of the descending colon supplied by the caudal mesenteric artery was identified and isolated by dividing the marginal artery at the limits of its territory, and the bowel flush at the same level. The aorta was then cleared below the renal vessels and a ligature was placed distal to the origin of the caudal mesenteric artery. All direct aortic branches—mostly lumbar arteries—to this level were ligated (*Figure 1*).

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Table 1 In vivo *reproducibility: LD readings at an equivalent colonic site in six individuals*

Experiment no.	Band-width (kHz)	Gain	LDV (mean ± s.d.) (V)	Coefficient of variation (%)
1	12	1	35·3 ± 12·7	36·0
2	12	1	48·0 ± 5·7	11·8
3	12	1	29·3 ± 5·5	18·7
4	12	1	72·8 ± 16·5	22·7
5	4	3	85·3 ± 4·1	4·8
6	12	1	48·3 ± 8·7	17·9

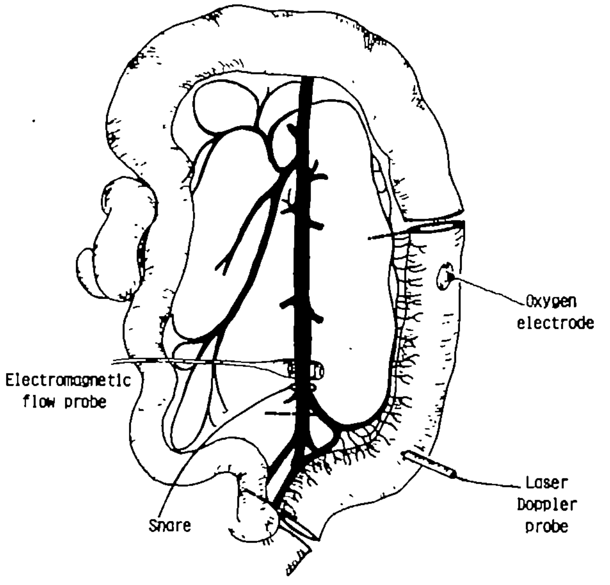

Figure 1 *Experimental preparation for flux and oximetry measurements with variable arterial inflow*

Flow in the caudal mesenteric artery was measured using a 2·5 mm electromagnetic flow probe (Gould Electronics SP2204), and shown to be the same as flow in the aorta, using a 4·5 mm flow probe. Thereafter, flow was monitored in the aorta. A snare was placed distal to the probe, and inflow to the colon varied (1–38 ml/min).

Six laser Doppler measurements were made from the midpoint of the colonic loop at each flow and mean flux plotted against arterial inflow (*Figure 2*). A significant correlation was found between arterial inflow and flux, $0\cdot01 > P > 0\cdot001$ (Student's *t* test).

Comparison of oximetry with laser Doppler readings

An oxygen electrode (Simonsen & Weel) was fixed to the serosal surface of the bowel, via the fluid well, which was held in place with tissue cement. The probe was unheated, as the endoscopic laser Doppler probe cannot be heated, thus both sets of readings were made at 37°C. As inflow was varied, oximetry readings were recorded, then plotted against LD (*Figure 3*). Again, a significant correlation was obtained between the two variables $0\cdot02 > P > 0\cdot01$ (Student's *t* test).

Discussion

Readings from the laser Doppler are highly reproducible experimentally, which we have confirmed using a stable emulsion. Biological systems are influenced by many independent variables, and the variability of our measurements in isolated colon rose to 16·9 per cent. Isotope clearance techniques have reported variabilities of 12·9 per cent[3] while variability for microsphere methods may be up to 15 per cent[4], although some workers have found microsphere variability to be as high as 60 per cent[5]. As part of the reproducibility study we compared stability of readings using different frequency limits (bandwidths), and found both to be equally accurate. Thus, in the animal experiment, we chose that setting (12 kHz) which gave the maximum deflection for the tissue under study.

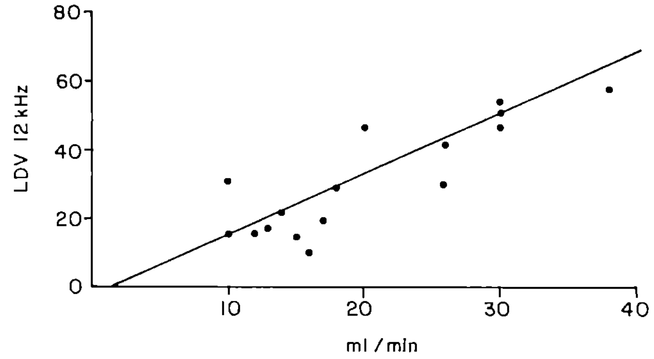

Figure 2 *Variations in arterial blood flow plotted against laser Doppler flux*

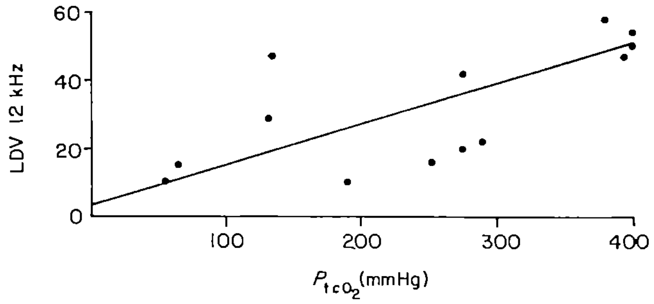

Figure 3 *Serosal oximetry readings plotted against laser Doppler with varying arterial inflow*

When the probe was hand-held, there was sometimes a delay until there were no further extraneous movements of the optical fibre before steady readings were obtainable[6], yet when the probe was stabilized within the biopsy channel of the endoscope, readings were more rapidly obtained and showed less variability. Furthermore, good correlation was found between arterial inflow and laser Doppler flux, showing that the instrument registers quickly and accurately acute events within one individual.

Controversy exists in the literature about the depth of penetration of the laser in bowel; the manufacturer claims that the incident light penetrates tissue to a depth of 1–1·5 mm[7]. Using an isotope washout technique, blood flow in intestinal wall has been shown to vary according to the histological level[8]. Using an alternative laser Doppler instrument (MedPacific), Shepherd and Riedel claimed that in the dog, flow was recorded only from the surface layers of bowel[9]. This has recently been challenged by other workers, using the Periflux, who suggested that at least in feline small intestine laser Doppler readings reflect flow in the entire bowel wall[10]. Our results in dog colon, showing that serosal and mucosal values are not significantly different, support this second view. This discrepancy in findings may be due to a difference in the instruments themselves, but supports the use of the Periflux endoscopically to assess blood flow in patients.

We noted a trend towards increasing flux nearer the rectum which did not reach statistical significance ($0\cdot1 > P > 0\cdot05$, Student's *t* test), possibly because of insufficient numbers. Significant variation in blood flow within one organ has been reported recently[11], but there are as yet no studies on the human colon.

Capillary circulation is known to be affected by invasive methods of measuring tissue blood flow[12] and we therefore chose to compare laser Doppler with oximetry because both are non-invasive. Shandall has shown experimentally that oxygen tension in the colon relates closely to tissue blood flow, and can predict healing of anastomoses[13]. A significant association between flux and oxygen tension was demonstrated, but was not absolute since oxygen tension depends on metabolic variables as well as tissue perfusion. Comparison with the radioactive xenon washout technique failed to demonstrate reproducible results because of the difficulty of placing the injection of xenon accurately within the bowel wall, the instability of the isotope in saline solution and its affinity for fat in the bowel mesentery.

This new endoscopic method now seems appropriate for use in patients and we are currently mapping gastrointestinal blood flow in normal volunteers with a view to studying the effect of pathological states and therapeutic manoeuvres on capillary circulation.

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References

1. Watkins D, Holloway GA Jnr. An instrument to measure cutaneous blood flow using the Doppler shift of laser light. *IEEE Trans Biomed Eng* 1978; **25**: 28–33.
2. Nilsson GE, Tenland T, Oberg PA. Evaluation of a laser Doppler flowmeter for measurement of tissue blood flow. *IEEE Trans Biomed Eng* 1980; **27**: 597–604.
3. Forrester DW, Spence VA, Walker WF. The measurement of colonic mucosal–submucosal blood flow in man. *J Physiol* 1980; **299**: 1–11.
4. Hales JRS. Radioactive microsphere techniques for studies of the circulation. *Clin Exp Pharm Physiol* 1974; Suppl 1: 31–46.
5. Neutze JM, Wyler F, Rudolph AM. Use of radioactive microspheres to assess distribution of cardiac output in rabbits. *Am J Physiol* 1968; **215**; 486–95.
6. Feld AD, Fondacaro JD, Holloway GA Jnr, Jacobson ED. Laser Doppler velocimetry: a new technique for the measurement of intestinal mucosal blood flow. *Gastro Endoscopy* 1984; **30**: 225–30.
7. Perimed KB, Stockholm. *Periflux PF2 User's Handbook* 1985; Ed 1: 11.
8. Kampp M, Lundgren D. Blood flow and flow distribution in the small intestine of the cat as analysed by the Kr^{85} washout technique. *Acta Physiol Scand* 1968; **72**: 282–97.
9. Shepherd AP, Riedel GL. Continuous measurement of intestinal mucosal blood flow by laser Doppler velocimetry. *Am J Physiol* 1982; **242**: 6668–72.
10. Ahn H, Lindhagen J, Nilsson GE, Salerud EG, Jodal M, Lundgren D. Evaluation of laser Doppler flowmetry in the assessment of intestinal blood flow in cat. *Gastroenterology* 1985; **88**: 951–7.
11. Ahn HC. Measurement of gastrointestinal blood flow with laser Doppler flowmetry. Linkoping University Medical Dissertation No. 226 1986; 135.
12. Holloway GA Jnr. Cutaneous blood flow responses to injection trauma measured by laser Doppler flowmetry. *J Invest Dermatol* 1980; **74**: 1–4.
13. Shandall A, Lowndes R, Young HL. Colonic anastomosis healing and oxygen tension. *Br J Surg* 1985; **72**: 606–9.

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Prospective 14- to 18-year follow-up study after parietal cell vagotomy

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One hundred and thirty-five patients underwent elective parietal cell vagotomy for duodenal, pyloric or prepyloric ulcers. The patients were followed prospectively at intervals of 1–3 years in order to detect postvagotomy symptoms and recurrent ulcers; 14–18 years after surgery 106 patients were studied with regard to recurrent ulceration and 84 concerning postvagotomy symptoms. Thirty-two patients (30 per cent) had developed proven recurrent ulcers and a further 9 per cent were suspected of having recurrences. Two patients were reoperated for gastric outlet obstruction and one for bile reflux gastritis. Four patients had severe dyspeptic symptoms and four severe dyspepsia plus dumping. No patient had severe diarrhoea. Forty-three patients were regarded as failures after parietal cell vagotomy. After treatment of these failures 88 per cent of the patients available for subsequent follow-up had satisfactory results. The alternatives to parietal cell vagotomy are discussed. It is concluded that although parietal cell vagotomy has a high long-term recurrence rate, this disadvantage is outweighed by the low incidence severe postvagotomy symptoms.

Keywords: Duodenal ulcer, parietal cell vagotomy, recurrent ulcer, dumping, postvagotomy diarrhoea

The first parietal cell vagotomies (PCV) without drainage for the treatment of duodenal ulcer were performed simultaneously in this department and in Leeds in 1969[1,2]. The operation evoked much interest because of its elegant use of applied anatomy and physiology. Rather than removing part of the stomach or denervating the entire stomach and other intra-abdominal organs, PCV enabled the surgeon selectively to denervate the acid secreting parietal cell mass yet obviated denervation of the antrum and pylorus. An apparently ideal situation was thus achieved in which acid secretion was reduced while preserving the reservoir and emptying functions of the stomach. A drainage procedure could be avoided thereby minimizing the chances of dumping, diarrhoea and bile reflux gastritis.

The original promise of reducing postvagotomy symptoms seems to have been fulfilled, but unfortunately the operation has been tainted by a high ulcer recurrence rate which increases with time. Many reports of short follow-up after PCV have been published recently[3–12], but only long-term studies can contribute to a meaningful evaluation of the place of PCV in the treatment of duodenal ulcer.

We present here what is believed to be the longest recorded follow-up study after PCV.

Patients and methods

Between March 1969 and April 1973, 135 patients underwent elective PCV for duodenal, pyloric or prepyloric ulcers. No patient had pyloric stenosis and none had a drainage procedure. The operative technique was as previously described[1]. There were no postoperative deaths. The patients were followed prospectively at intervals of 1–3 years by direct interview or by postal questionnaire. Questions were aimed at detecting postvagotomy symptoms and recurrent ulcers. Patients with symptoms suggesting recurrent ulcers were gastroscoped. By April 1987, 15 patients had undergone a second gastric operation for various reasons. Thirty-one others had died. The remaining 89 patients were called in for interview. Forty-eight responded and were interviewed at a clinic visit. Eighteen further patients were interviewed by telephone and 18 others answered a postal questionnaire. Five patients could not be traced. Thus the follow-up rate of the live patients (excluding the 15 patients who had had a second operation and are considered separately) was 84 out of 89 (94 per cent). These 84 patients had been followed up for between 14 and 18 years (mean 15·5 years) and were questioned about ulcer-like pain, nausea, vomiting, heartburn, diet, appetite, postprandial fullness, weight loss, dumping, diarrhoea, use of ulcer medication, use of ulcerogenic drugs, smoking and alcohol consumption. All symptomatic patients were encouraged to undergo gastroscopy. Forty asymptomatic patients who were reviewed in the clinic were also offered a gastroscopy.

Although only 84 patients were available for follow-up of postvagotomy symptoms by April 1987, 106 patients could be studied with regard to recurrent ulceration. Among the 31 patients who had died, three had developed recurrent ulcers at earlier follow-up and are included in the study. Another six patients were considered to have died without recurrent ulcers; one died soon after a gastrectomy for gastric carcinoma 13 years after PCV, two died within one month of their last interview and three others died within three months of their last contact with us and no ulcer was found at post-mortem examination. These six patients are also included in the study. Of the five patients who could not be contacted, one had had a new ulcer diagnosed before being lost and is included in the study. Twelve other patients had been reoperated for recurrent ulceration and are included in the study of recurrent ulcers but excluded from the assessment of postvagotomy symptoms. Thus 26 patients in all had been lost from the long-term study of recurrence. These 26 had been previously followed for between one month and 13 years (mean 6 years) and will not be considered further. Of the 109 remaining patients (*Table 1*), three had undergone a second gastric operation during the study period for reasons other than recurrent ulceration between 1 and 8 years after their original operation without a recurrent ulcer having been diagnosed between the two operations. These three are also not considered further in the context of recurrent ulceration.

In summary, 106 patients were available for study of recurrent ulceration and 84 for assessment of postvagotomy complications at 14–18 years after PCV.

Results

Recurrent ulceration

Thirty-two of the 106 patients (30 per cent) developed recurrent ulcers in the study period. The recurrences were diagnosed from 2 months to 16 years after PCV (mean 7 years). Thirteen of

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Table 1 *Details of 109 patients*

Sex (M:F)	3·7:1
Age (years)	
Mean 46	
Range 21–81	
Site	
Duodenal	64
Pyloric/prepyloric	45
History (years)	
<2	10
2–45	99
Previous complications	
Perforation	8
Haemorrhage	29
Both	4
Surgeon	
Consultant	35
Registrar	74

Table 2 *Incidence of complications and symptoms*

Complication	No.*	Severe/ frequent	Mild/ moderate/ occasional
Gastric outlet obstruction	135	2	—
Bile reflux gastritis	85	1	—
Dumping	84	3	15
Diarrhoea	84	0	12
Post-prandial fullness	84	0	16
Ulcer-like pain	68	6	11
Nausea/vomiting	68	4	12
Heartburn	68	5	15

* Patients available for study (see text).

the recurrences occurred 10–17 years after surgery and only ten within 5 years of operation. There was no difference in the recurrence rates when PCV was used for duodenal ulcers compared with pyloric/prepyloric ulcers or when the operation was performed by a consultant surgeon or by a registrar.

The ulcers were diagnosed gastroscopically in 26 patients, radiologically in five and at post-mortem examination in one. The recurrent ulcers were duodenal in nine, pyloric or prepyloric in ten and gastric in eight patients. In five patients the site was not recorded.

In 12 patients the recurrent ulcer was treated by antrectomy and 20 patients received medical treatment, usually H_2 receptor blockers. We divided the recurrent ulcers into two groups, 'innocuous' and 'malevolent'. Innocuous ulcers (6 patients) were those which responded to a single course of anti-ulcer treatment and did not recur in the subsequent follow-up period. Malevolent ulcers were those which did not respond to medical treatment and subsequently required surgery (12 patients), those which presented with severe bleeding (1 patient), those which recurred after a successful course of treatment (5 patients) or those which required treatment with long-term or permanent anti-ulcer treatment because of persisting symptoms (5 patients). Three patients could not be classified because follow-up was too short. Thus 6 of 29 ulcers were innocuous and 23 malevolent.

In addition to the 32 patients with proven recurrent ulcers, eight patients had current symptoms of a new ulcer. Four of these refused gastroscopy and in the other four no ulcer was found at gastroscopy. A further five patients had had symptoms of recurrence at some time in the past, but they had received anti-ulcer treatment from their general practitioners without having been investigated. Thus nine extra patients may have had undiagnosed recurrences. Twelve asymptomatic patients were examined gastroscopically and no ulcers were found.

Postvagotomy symptoms (*Table 2*)

As opposed to the investigation into recurrent ulcers where 106 patients were studied, the following section deals only with the 84 patients available for review 14–18 years after PCV, plus three patients operated upon for gastric retention and bile reflux gastritis. Excluded are four patients with recurrent ulcers who were treated medically but were subsequently lost to follow-up before 14 years. The 12 patients reoperated for recurrent ulcer and the six patients who were judged to have had no recurrence of ulceration before they died are also omitted. Included are the 16 patients with medically treated recurrent ulcers who were followed for 14–18 years after PCV. In the assessment of pain, nausea, vomiting and heartburn, there are only 68 patients however, since the latter 16 patients have been excluded because many of them were currently receiving anti-ulcer treatment and they are considered later.

Two patients were operated on for gastric outlet obstruction 14 and 21 months after PCV. One patient was operated on for severe reflux gastritis eight years after his original operation. In addition to the symptoms listed in *Table 2*, 12 out of 84 patients had lost more than 5 kg in weight, 14 had a diminished appetite and five kept a special diet to prevent various postvagotomy symptoms.

Visick grading (*Tables 3 and 4*)

Of the 107 patients shown in *Table 1*, 103 could be given a Visick grading. Excluded are the six patients who were judged to have had no recurrence before they died but in whom information about postvagotomy symptoms was lacking. The modified Visick classification suggested by Goligher *et al.*[13] was used.

The eight patients graded Visick IV for ulcer-like dyspepsia had the following features: five used salicylate tablets daily and of these five, one took steroid tablets daily as well. The sixth patient smoked 40 cigarettes a day. The remaining two patients drank three beers and smoked 20 cigarettes daily. All eight patients were offered a gastroscopy. Four refused and the remainder were examined gastroscopically. One had a hiatus hernia with reflux oesophagitis and another had multiple superficial antral ulcers presumably due to salicylate abuse. Two patients had no abnormalities on gastroscopy.

The following features are noteworthy: only one patient had bile reflux gastritis and no patient had severe diarrhoea. While four patients had severe dumping, in none was this the only cause of a Visick IV grading. The incidence of severe postvagotomy symptoms was only 9 per cent. Postprandial fullness, weight loss and the need for special diet were uncommon.

Visick grading after treatment of failures. Of the 43 patients classified Visick IV, 35 have been treated, 15 surgically and 20 medically. Eight patients are currently being treated for dyspeptic symptoms. Seven patients have been lost to follow-up after treatment of their complications. Thus 88 patients could be given a revised Visick grading (*Table 5*).

Table 3 *Visick grading* (*103 patients*)

I	30
II	29
III	1
IV	43

Table 4 *Reasons for Visick IV grading*

Recurrent ulcers	32
Bile reflux gastritis	1
Gastric retention	2
Dyspeptic symptoms	4
Dyspepsia plus dumping	4
Total	43

Table 5 *Visick grading after treatment of 35 failures (88 patients)*

Grade I	40
Grade II	36
Grade III	2
Grade IV	10
No follow-up	15

Gastric cancer

Two patients developed gastric cancer after PCV. One underwent a gastrectomy 13 years after his original operation. In the second patient a gastric cancer was found at post-mortem examination six years after PCV. A third patient died 5 years after PCV with disseminated carcinoma. The primary site of the tumour is unknown.

Discussion

This study reveals a 30 per cent proven recurrent ulcer rate 14–18 years after PCV. A further 9 per cent of the patients might have had recurrences but were not examined gastroscopically. Before rejecting PCV out of hand, this disappointing result has to be placed in perspective by comparing our results with those following the other standard operations for duodenal ulcer, namely truncal vagotomy and drainage (TVD), selective vagotomy and drainage (SVD) and vagotomy and antrectomy (VA), as well as with the obsolete operation gastrectomy without vagotomy.

There is unfortunately a dearth of prospective long-term follow-up studies after these operations. Short-term retrospective studies tend to reveal a deceptively low recurrence rate. For TVD recurrence rates of 25–28 per cent 10–15 years after operation have been reported[14,15], but it may be as low as 9 per cent[13]. As far as SVD is concerned really long-term results are not available but the figure may reach 17–20 per cent after only five years[5,16]. Vagotomy and antrectomy is much more successful in curing the ulcer than vagotomy alone. The ulcer recurrence rate is 0–5 per cent in follow-up studies of 4–16 years[6,9,11,13,17–19]. An especially long-term study reveals a 2·6 per cent recurrence rate 22–30 years after gastrectomy alone[20] but reports of a 14 per cent late recurrence rate also exist[21].

Therefore if the ulcer recurrence rate is taken as the only criterion for judging which operation to choose, there is no doubt that VA is the procedure of choice. However, as Goligher *et al.*[13] have stated 'it would be preferable to have several recurrent ulcers ... than to incur a single operative death'. The operative mortality rate after PCV was zero in our report and is given as 0·3 per cent in collected series[9]. The mortality following VA ranges between 0 and 2 per cent[6,9,11,13,17,18]. The mortality figure for VA may in fact be biased in favour of VA if one considers that a surgeon may often choose to do a vagotomy and drainage procedure rather than antrectomy if circumstances surrounding the duodenum, for example a deeply penetrating ulcer, make antrectomy particularly hazardous[13,17].

Other factors which speak against VA as the routine operation for duodenal ulcer include the incidence of postgastrectomy symptoms. Patients after VA suffer moderate to severe dumping, diarrhoea, dyspepsia, postprandial fullness, bile reflux gastritis and weight loss in 17–38 per cent of cases in long-term studies[11,13,16,17,18]. Our incidence of these problems was 9 per cent. Recurrent ulcers are relatively easy to treat while postgastrectomy symptoms are notoriously difficult to manage[5,6,11] and any series of gastrectomy patients will include a number of intractable 'gastric cripples'. A fivefold increase in suicide among gastrectomy patients compared with the normal population has been described[22]. The reasons for this are unknown. There were no suicides among our patients.

If one could tailor the operation to fit the individual patient, the ideal situation would be achieved: namely, choose VA for patients at high risk of developing a recurrent ulcer and PCV for those with a low risk. This approach has been studied by numerous surgeons but no unequivocal solution has emerged. It is claimed by some and refuted by others that patients in the high risk group are young patients, men, those with long histories, patients with pyloric or prepyloric ulcers, high acid secretors, smokers, alcoholics and those with previous bleeding or perforation[3–5,8,10,12,17,23–28]. Neither the site of the ulcer nor the experience of the surgeon made any difference to the recurrence rate in the present report. It has been previously claimed by us and others that the recurrent ulcers after PCV are 'benign'[5,7,23,24] and easy to treat. Our present experience shows that almost 90 per cent of the recurrent ulcers were malevolent rather than innocuous and required surgery or prolonged medical treatment.

A word must be added about asymptomatic recurrences. Blackett and Johnston[23] stated that 'no doubt the incidence of recurrence ... would have been higher if we had routinely endoscoped asymptomatic patients'. We encouraged all our patients to undergo gastroscopy even when they had no symptoms. Only one-quarter of the asymptomatic patients reviewed at the clinic consented to gastroscopy. None of the twelve had a recurrent ulcer.

'Every operation for duodenal ulcer is a success until it is found out'[28]. Is it time to ring the death knell for PCV? Looking solely at the recurrence rate one would be forced to say yes. However, when one regards the 88 per cent of patients who were finally happy with their operation, in some cases after treatment of failure, compared with the high incidence of gastric cripples after gastrectomy, one would be inclined to answer negatively especially if some way of tailoring the operation to the needs of the patient can be found in the future.

References

1. Amdrup E, Jensen H-E. Selective vagotomy of the parietal cell mass preserving innervation of the undrained antrum. *Gastroenterology* 1970; **59**: 522–7.
2. Johnston D, Wilkinson A. Selective vagotomy with innervated antrum without drainage procedure for duodenal ulcer. *Br J Surg* 1969; **56**: 626.
3. Enskog L, Rydberg B, Adami H-O, Enander LK, Ingvar C. Clinical results 1–10 years after highly selective vagotomy in 306 patients with prepyloric and duodenal ulcer disease. *Br J Surg* 1986; **73**: 357–60.
4. Clark CG, Fresini A, Araujo JGC, Boulos PB. Proximal gastric vagotomy or truncal vagotomy and drainage for chronic duodenal ulcer? *Br J Surg* 1986; **73**: 298–300.
5. Hoffmann J, Jensen H-E, Schulze S, Poulsen PE, Christiansen J. Prospective controlled vagotomy trial for duodenal ulcer: Results after five years. *Br J Surg* 1984; **71**: 582–5.
6. Donahue PE, Bombeck J, Condon RE, Nyhus LM. Proximal gastric vagotomy versus selective vagotomy with antrectomy: Results of a prospective, randomized clinical trial after four to twelve years. *Surgery* 1984; **96**: 585–91.
7. Knight CD, Van Heerden JA, Kelly KA. Proximal gastric vagotomy. *Ann Surg* 1983; **197**: 22–6.
8. Fraser AG, Brunt PW, Matheson NA. A comparison of highly selective vagotomy with truncal vagotomy and pyloroplasty—one surgeon's results after 5 years. *Br J Surg* 1983; **70**: 485–8.
9. Koo J, Lam SK, Chan P, Lee NW, Wong J, Ong GB. Proximal gastric vagotomy, truncal vagotomy with drainage and truncal vagotomy with antrectomy for chronic duodenal ulcer. *Ann Surg* 1983; **197**: 265–71.
10. Jensen H-E, Kjaergaard J, Meisner S. Ulcer recurrence two to twelve years after parietal cell vagotomy for duodenal ulcer. *Surgery* 1983; **94**: 802–6.
11. Gleysteen JJ, Condon RE, Tapper EJ. Prospective trial of proximal gastric vagotomy. *Surgery* 1983; **94**: 15–20.
12. Koffman CG, Hay DJ, Ganguli PC *et al.* A prospective randomized trial of vagotomy in chronic duodenal ulceration: 4-year follow-up. *Br J Surg* 1983; **70**: 342–5.
13. Goligher JC, Feather DB, Hall R *et al.* Several standard elective

operations for duodenal ulcer. Ten to 16 year clinical results. *Ann Surg* 1979; **189**: 18–24.
14. Stempien SJ, Dagradi AE, Lee ER, Simonton JH. Status of duodenal ulcer patients ten years or more after vagotomy-pyloroplasty. *Am J Gastroenterol* 1971; **56**: 99–108.
15. Nobles ER Jr. Vagotomy and gastroenterostomy. 15-year follow-up of 175 patients. *Am Surg* 1966; **32**: 177–82.
16. Højlund B, Madsen P. The clinical results of selective vagotomy and pyloroplasty six to nine years later. *Dan Med Bull* 1980; **27**: 164–7.
17. Mulholland M, Morrow C, Dunn DH, Schwartz ML, Humprey EW. Surgical treatment of duodenal ulcer. *Arch Surg* 1982; **117**: 393–7.
18. Jackson DS, Smith EEJ, Spencer J, De Vries BS, Alexander-Williams J, Dorricott NJ. Proximal gastric vagotomy or truncal vagotomy and antrectomy for chronic duodenal ulcer—5–7 year results of a prospective randomized multicentre trial. *Br J Surg* 1982; **69**: 282.
19. Sawyers JL, Herrington JL, Burney DP. Proximal gastric vagotomy compared with vagotomy and antrectomy and selective gastric vagotomy and pyloroplasty. *Ann Surg* 1977; **186**: 510–17.
20. Fischer AB. Twenty-five years after Billroth II gastrectomy for duodenal ulcer. *World J Surg* 1984; **8**: 293–302.
21. Postlethwait RW. Retrospective study of operations for peptic ulcer. *Surg Gynecol Obstet* 1979; **149**: 703–8.
22. Fischer AB, Knop J, Graem N. Late mortality following Billroth II resection for duodenal ulcer. *Acta Chir Scand* 1985; **151**: 43–7.
23. Blackett RL, Johnston D. Recurrent ulceration after highly selective vagotomy for duodenal ulcer. *Br J Surg* 1981; **68**: 705–10.
24. Busman DC, Munting TDK. Results of highly selective vagotomy in a non-university teaching hospital. *Br J Surg* 1982; **69**: 820–4.
25. Poppen B, Delin A. Parietal cell vagotomy for duodenal and pyloric ulcers. *Am J Surg* 1981; **141**: 323–9.
26. Andersen D, Amdrup E, Høstrup H, Sørensen FH. The Aarhus County vagotomy trial: trends in the problem of recurrent ulcer after parietal cell vagotomy and selective gastric vagotomy with drainage. *World J Surg* 1982; **6**: 86–92.
27. Ørnsholt J, Amdrup E, Andersen D, Høstrup H. Aarhus County vagotomy trial: ulcer recurrence rate related to alterations in gastric acid secretion after selective gastric and parietal cell vagotomy. *Scand J Gastroenterol* 1983; **18**: 465–72.
28. Editorial. Peptic ulceration: the eye of the cyclone. *Lancet* 1986; **ii**: 1015–16.

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Hyperthyroidism and hypothyroidism complicating the treatment of thyrotoxicosis

Three separate studies of recurrent hyperthyroidism and hypothyroidism in groups of patients treated for thyrotoxicosis by anti-thyroid drugs, surgery and radioiodine are presented. The incidence is compared in the three groups. Two hundred and fifty-three patients with primary thyrotoxicosis received a year-long course of anti-thyroid drugs: 43 per cent relapsed in the first year following the completion of treatment. Of those remaining euthyroid at the beginning of the second year after treatment a further 21 per cent relapsed during that year and in subsequent years, 21 per cent, 18 per cent and 13 per cent of those remaining euthyroid at the start of the third, fourth and fifth years relapsed. Of those followed for the full 5 years 26 per cent remained in remission and 74 per cent had relapsed over this period. After bilateral subtotal thyroidectomy for thyrotoxicosis in 146 patients, 19 per cent were hypothyroid and 1·4 per cent had relapsed 18 months after surgery. The incidence of postoperative hypothyroidism was lower in the younger patients (under 25 years). The absence of thyroid auto-antibodies preoperatively is an indication of a favourable result. The histological recognition of lymphocytic infiltration in the gland and the presence of thyroid auto-antibodies indicated an unfavourable outcome. Radioactive iodine gave an unpredictable response at therapeutic doses with 24 per cent relapsing in the first year after treatment. With ablative doses of radioactive iodine the incidence of hypothyroidism reached 94 per cent at 5 years after treatment. Surgery gives the best long-term results of the three treatment options and is the treatment of choice for the young, the severely toxic and those with toxic multinodular goitre.

Keywords: Hyperthyroidism, hypothyroidism, thyrotoxicosis, thyroid auto-antibodies

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Thyrotoxicosis is a common condition affecting between 1·9 and 2·7 per cent of the female population and between 0·16 and 0·23 per cent of the male population[1].

Three forms of therapy are available: antithyroid drugs, bilateral subtotal thyroidectomy and radioactive iodine (^{131}I). None of these is ideal and all share the same complications of recurrent hyperthyroidism and permanent hypothyroidism after treatment. This study demonstrates the incidence of recurrent hyperthyroidism in 253 patients treated with long-term antithyroid drugs and compares the incidence of recurrent hyperthyroidism and permanent hypothyroidism in 146 patients treated surgically, with 89 patients given a therapeutic dose of ^{131}I and 57 patients treated with ablative doses of ^{131}I.

Patients and methods

Antithyroid drug treatment

Two hundred and fifty-three patients with thyrotoxicosis received a full year's course of antithyroid drugs. Carbimazole 45 mg daily was administered until the patients were euthyroid and then 15 mg daily was given with T3 supplement for the remainder of the year. The patients were followed for 5 years and the incidence of relapse was measured in relation to the number of patients who were euthyroid at the start of each year for 5 years.

Surgical treatment

A total of 146 patients (23 male and 123 female) ranging in age from 15 to 75 years, underwent bilateral subtotal thyroidectomy when euthyroid after either antithyroid drug therapy or a combination of propranolol and Lugol's iodine. The technique used was the same in all cases. All four thyroid arteries were ligated, the superior thyroid arteries being divided. The pyramidal lobe was completely removed and in no case were the strap muscles divided. The remnants were judged by eye, designed to be roughly 5 g on each side for the patients with diffuse hyperplasia and with larger remnants for those with a toxic multinodular goitre. The recurrent laryngeal nerves were not formally dissected. The remnants were sutured to the tracheal fascia on each side. Suction drains were placed lateral to each remnant and remained in position for 24 h postoperatively. The skin was closed using skin clips without suture of the subcutaneous layer. All clips were removed by 72 h postoperatively. The average stay in hospital was 5 days after surgery.

Radioactive iodine

Therapeutic doses of radioactive iodine (^{131}I, 185–296 MBq, 5–8 mCi) were received by 89 patients and 57 patients received ablative doses (740–925 MBq, 20–28 mCi); all were followed up for 5 years, the annual incidence of hypothyroidism or relapse being recorded.

Results

Antithyroid drug treatment

After the administration of antithyroid drugs for a full year there is a relapse rate of 43 per cent in the first year after completion of the course. In the subsequent years to 5 years, 21 per cent, 21 per cent, 18 per cent and 13 per cent of those remaining euthyroid at the start of each year relapsed (*Figure 1*). Expressing these results in a different way, by 5 years 74 per cent have relapsed and 26 per cent remain in remission.

Surgical treatment

The incidence of hypothyroidism in the 146 patients undergoing bilateral subtotal thyroidectomy is shown in *Figure 2*. The

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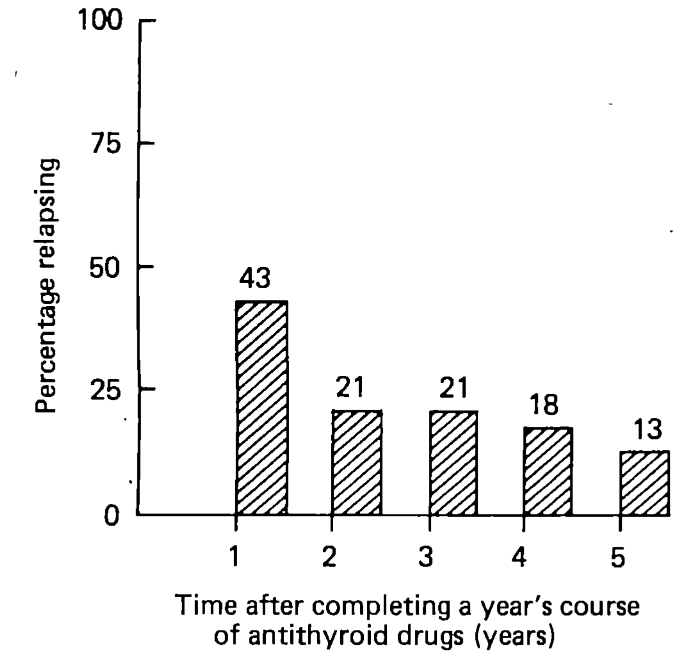

Figure 1 *Rate of relapse (recurrent hyperthyroidism) in 253 patients following a full year's course of antithyroid drugs*

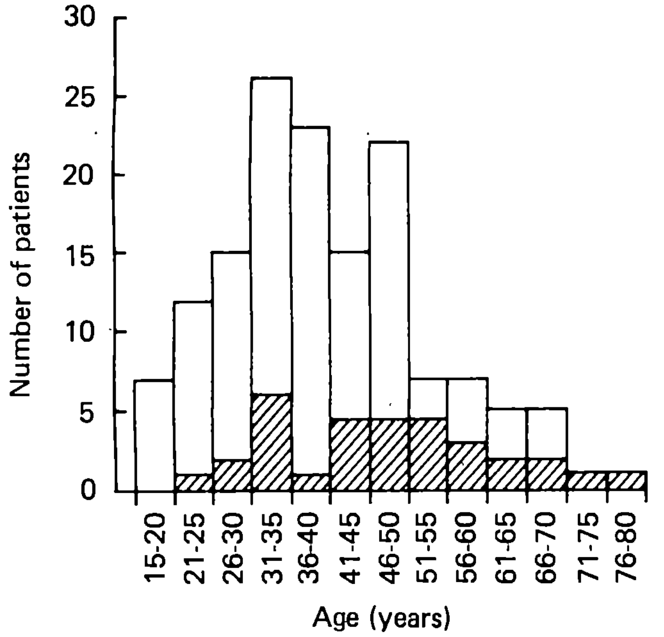

Figure 2 *Age distribution of 146 (23 males and 123 females) patients undergoing bilateral subtotal thyroidectomy for thyrotoxicosis.* ▨, *hypothyroid within 18 months of surgery;* ☐, *euthyroid*

overall incidence is 19 per cent at 18 months after surgery. For patients with primary thyrotoxicosis with diffuse hyperplasia of the gland the incidence is 18 per cent and for those with secondary thyrotoxicosis due to a toxic multinodular goitre it is 25 per cent. The incidence of recurrent hyperthyroidism at 18 months is 1·4 per cent.

Table 1 shows the incidence of hypothyroidism at 18 months after surgery in relation to age and *Table 2* shows the incidence in patients with primary and secondary thyrotoxicosis.

Studying the patients in whom pre-operative thyroid antibody studies were carried out, all of those who became hypothyroid at 18 months had positive titres of thyroid microsomal or thyroglobulin antibodies. For microsomal antibodies a dilution greater than 1:100 and for thyroglobulin antibodies greater than 1:10 is taken as positive. It was, however, also observed that 52 per cent of those who remained euthyroid at 18 months had positive antibody titres.

Although these data are difficult to quantitate it was observed that when the histology of the gland removed showed lymphocytic infiltration there was an increased incidence of hypothyroidism, and when this histological feature was absent it was an indication of a favourable result.

No patient in the series received a blood transfusion after surgery and no patient required a second operation for the release of a haematoma.

Radioactive iodine treatment

Of the 89 patients who received a therapeutic dose of radioactive iodine (^{131}I), 48 per cent were euthyroid 1 year after treatment, 28 per cent were hypothyroid but 26 per cent had relapsed. Of the 57 patients who received ablative doses of radioactive iodine (740–925 MBq, 20–28 mCi), 2 relapsed and the remainder were hypothyroid by 5 years after treatment (*Figure 3*).

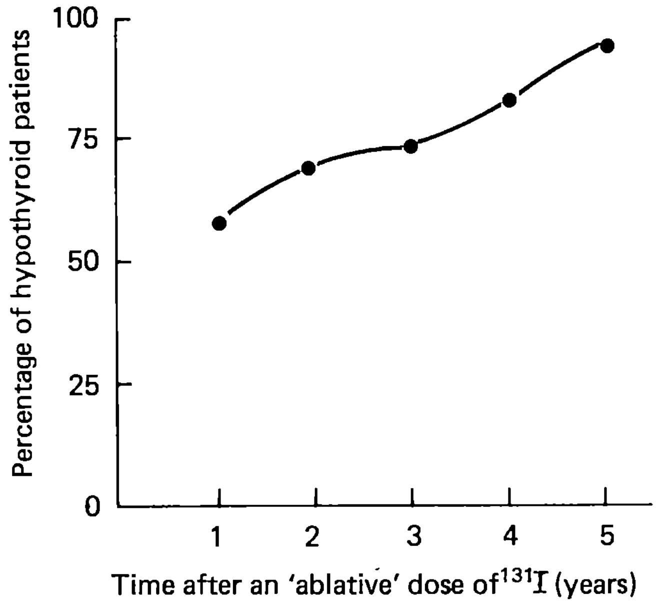

Figure 3 *Incidence of hypothyroidism in 57 patients following an ablative dose of* ^{131}I *(740–925 MBq)*

Table 1 *Incidence of hypothyroidism complicating bilateral subtotal thyroidectomy for Graves' disease (primary thyrotoxicosis)*

Age	Percentage hypothyroid 18 months after surgery
<20	0
21–30	12
31–40	15
41–50	25
>50	25

Table 2 *Incidence of postoperative hypothyroidism in 146 patients undergoing bilateral subtotal thyroidectomy for thyrotoxicosis*

Patient characteristics	Percentage
Overall incidence (146)	19
Toxic multinodular goitre (28) (secondary thyrotoxicosis)	25
Graves' disease (118) (primary thyrotoxicosis)	18

Discussion

There are three separate groups of patients in this study. In the series of patients with primary hyperthyroidism who received antithyroid drugs for a year the incidence of relapse over a 5-year period is 74 per cent with 26 per cent remaining in remission. The incidence of relapse in patients with secondary thyrotoxicosis is known to be much higher.

Youth, mild symptoms, the return of the goitre to normal or near-normal size during treatment[2] and a short history of thyrotoxicosis have been listed as factors which indicate a favourable response to drug therapy. A large goitre, relapse after previous treatment (medical or surgical), a long history and the presence of ocular and cardiac symptoms have been cited as poor prognostic indicators[3].

Patients who are both HLA–DRw3 positive and who have TSH receptor antibodies at the time of drug withdrawal are more likely to relapse[4]. The initial severity of the disease emerges as the most important prognostic indicator in the patients reported in this series[5], although this factor has been found by other authors to be unhelpful[3,6]. The highest incidence of relapse after drug therapy (43 per cent) occurred in this series in the first year after treatment and similar figures have been reported by others[7].

Stege[8] recommends longer courses of antithyroid drugs if better long-term remission figures are to be obtained.

Surgery for thyrotoxicosis carries a low morbidity and zero mortality provided that strict rules are applied in patient management. The significant complications in the surgically treated group are recurrent hyperthyroidism and hypothyroidism. The figure of 18 per cent for those with primary hyperthyroidism and 25 per cent for those with secondary hyperthyroidism will increase over a 10-year period but there is general agreement that about 93 per cent of those patients who will develop hypothyroidism will do so by 18 months after surgery[9]. The relapse rate of 1·4 per cent at 18 months in this study is also likely to increase over the following 20 years[10,11].

In this series the size of the thyroid remnant has been judged by eye and tissue has not been weighed to assess the volume of the remnant. A wide range of remnant size is allowable[12], but a larger remnant has been left in those patients with toxic multinodular goitre.

Treatment with standard therapeutic doses of ^{131}I carries a variable but high risk of hypothyroidism, being about 20 per cent in the first year after treatment and rising to about 50 per cent after 10 years[13]. In this study there is a relapse rate of 24 per cent in the first year after treatment. The response therefore to therapeutic doses of radioactive iodine is unpredictable.

When ablative doses of radioactive iodine were used the incidence of hypothyroidism approached 100 per cent at 5 years after treatment but even at this dose (740–925 MBq, 20–28 mCi), two patients relapsed and a further dose of ^{131}I was given.

In conclusion, after bilateral subtotal thyroidectomy for thyrotoxicosis there is a modest incidence of hypothyroidism and a very low morbidity. Surgery is the treatment of choice in patients with severe thyrotoxicosis in view of the rapid response and treatment is recommended without a prolonged preoperative course of anti-thyroid drugs. It is also the treatment of choice in those patients with a large goitre, in the young and in those with a toxic multinodular goitre.

References

1. Tunbridge WMG, Evered DC, Hall R *et al.* The spectrum of thyroid disease in a community. The Whickham Survey. *Clin Endocrinol* 1977; 7: 481–93.
2. Solomon DH, Beck JC, Vanderlaan WP, Astwood EB. Prognosis of hyperthyroidism treated by antithyroid drugs. *JAMA* 1953; **152**: 201–5.
3. Barfred A. Methylthiouracil in the treatment of thyrotoxicosis. *Am J Med Sc* 1947; **214**: 349–61.
4. McGregor AM, Rees Smith B, Hale R, Petersen MM, Miller M, Dewar PJ. Prediction of relapse in hyperthyroid Graves' disease. *Lancet* 1980; **1**: 1101–3.
5. Sheldon J, Reid DJ. Thyrotoxicosis: changing trends in treatment. *Ann R Coll Surg Engl* 1986; **68**: 283–5.
6. Alexander WD, McLarty DG, Robertson J *et al.* Prediction of the long term results of antithyroid drug therapy for thyrotoxicosis. *J Clin Endocrinol Metab* 1970; **30**: 540–3.
7. Hershman JM, Givens JR, Cassidy CE, Ashwood EB. Long-term outcome of hyperthyroidism treated with antithyroid drugs. *J Clin Endocrinol* 1966; **26**: 803–7.
8. Stege R. Antithyroid drug therapy in hyperthyroidism. *Acta Chir Scand* (Suppl 501) 1980. .
9. Hedley AJ, Bewsher PD, Jones SJ *et al.* Late onset hypothyroidism after subtotal thyroidectomy for hyperthyroidism: implications for long term follow up. *Br J Surg* 1983; **70**: 740–3.
10. Surgrue DD, Drury MI, McEvoy M, Hefferman SJ, O'Malley E. Long-term follow up of hyperthyroid patients treated by subtotal thyroidectomy. *Br J Surg* 1983; **70**: 408–11.
11. Hamburger J. Recurrent hyperthyroidism after thyroidectomy. *Arch Surg* 1976; **111**: 91–2.
12. Tweedle D, Colling A, Schardt W *et al.* Hypothyroidism following partial thyroidectomy for thyrotoxicosis and its relationship to thyroid remnant size. *Br J Surg* 1977; **64**: 445–8.
13. Dunn JT, Chapman EM. Rising incidence of hypothyroidism after radioactive iodine therapy in thyrotoxicosis. *New Engl J Med* 1964; **271**: 1037–42.

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Short note

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The Rapignost-Amylase test in acute pancreatitis

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The concept of a simple, rapid bedside test to confirm acute pancreatitis is attractive but it must be reliable. Several studies have suggested that the Rapignost-Amylase test is highly sensitive and specific but they were based on small numbers or highly selected groups of patients. This prospective study compares the serum amylase estimation with the result of the test strips, under the same conditions and by the same personnel who are responsible for urine analysis.

Materials and methods

The Rapignost-Amylase test strip* colorimetrically detects an increase in urinary amylase. The depth of the purple colour is compared with a chart and the result classified as: −ve, normal; +ve, slightly raised; and ++ve, significantly raised urinary amylase. The serum amylase estimations were by the Phadebas Amylase Test†. Our laboratory defines the upper limit of normal as 300 units/l, but clinically a diagnosis of pancreatitis is supported by a value in excess of 1000 units/l.

Only patients admitted with acute abdominal pain were studied and only the first sample of urine passed after admission was tested. The admitting team did not change their normal practice and requested urgent serum amylase estimations only when indicated.

Results

Urine specimens from 306 patients were tested but the serum amylase was requested in only 218 of these cases. Of these 218, 41 had a serum amylase in excess of 1000 units/l and 26 patients had levels between 300 and 1000 units/l. The remaining 151 had a normal value.

Five patients had elevated urinary amylase with a normal serum amylase and a further five with a value between 300 and 1000 units/l. The false positive rate is therefore 10 out of 306−41; a specificity of 96 per cent.

Only 18 of the 41 patients with a serum amylase in excess of 1000 units/l had a significantly elevated urinary amylase and a further 9 had a slightly elevated urinary amylase. There were therefore 14 out of 41 false negative test strip estimations, a sensitivity of 66 per cent.

Discussion

Eighty-eight patients with a normal urinary amylase did not have the serum amylase determined but none of these patients had clinical evidence of acute pancreatitis so it is assumed that the test strip results were correct.

Table 1 *Numbers of patients grouped according to the urinary amylase test strip result*

Rapignost-Amylase result	Urine test only	Urine + serum	Serum amylase (units/l)		
			<300	300–1000	>1000
−	264	181	146	21	14
+	22	18	4	5	9
++	20	19	1	0	18
Total	306	218	151	26	41

The time interval between the onset of symptoms and the test being performed is important, as an earlier presentation favours an elevated serum and a normal urinary amylase. The majority (10/14) of false negative tests presented within 12 h of onset of their symptoms. Those authors who compared the test with serum amylase estimations[1,2] also commented on this.

Habenstein's[3] results of a 5 per cent false positive and 1 per cent false negative rate were derived from outpatient specimens, comparing the test result with two other methods of estimating the urinary amylase. A multicentre series of 1294 patients[4] was based on 'hospitalized patients and partly from outpatients'; the test was again compared with estimations of the urinary amylase.

Holdsworth's paper[5] compared the test with plasma amylase, finding a 100 per cent sensitivity and 78 per cent specificity and concluded that the test was of potential screening value. In this paper only 4 cases of clinically occult pancreatitis were found; 19 other positive test strips were from cases which had previously been diagnosed as acute pancreatitis.

Gunn[2] reported four negative test strips in eight patients with a serum amylase in excess of 1000 units/l and concluded that the test was unacceptable in a normal clinical setting.

This study compares a serum test with a urinary test and the serum and urinary levels of amylase peak at different times. The conclusion is however justified as comparison is being made between the standard screening test and the test strip, which is marketed as 'a useful screening test for acute pancreatitis'. The Rapignost-Amylase test is not suitable for screening patients for suspected acute pancreatitis as its sensitivity is only 66 per cent.

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References

1. Touquet VLR, Wilcox AH. The use of the Rapignost strip for estimating urinary amylase levels. *Arch Emerg Med* 1985; **2**: 165–9.
2. Gunn IR, Faye S, Clayton MGG. Prospective evaluation of urinary amylase test strip. *Lancet* 1986; **i** (letter): 1161.
3. Habenstein K, Kohl H. A new test strip for the determination of amylase in the urine. *J Clin Chem Clin Biochem* 1981; **19** (abstract): 688.
4. Oellerich M, Seiler D, Nagel D, Weidemann G, Weiss L *et al.* Test strip for the rapid detection of amylase in the urine. *Deutsche Medizinische Wochenschrift* 1983; **108**: 1308–11.
5. Holdsworth PJ, Mayer AD, Wilson DH, Flowers MW, McMahon MJ. A simple screening test for acute pancreatitis. *Br J Surg* 1984; **71**: 958–9.

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History of colorectal polypectomy and risk of subsequent colorectal cancer

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In a case control study, which formed part of a large, population-based investigation of the incidence, aetiology and survival of colorectal cancer, 24 of 715 cases and 4 of 727 age/sex group matched controls gave a past history of bowel polypectomy ($\chi^2_1 = 17$, $P < 0{\cdot}001$, relative risk = 6·37, 95 per cent confidence interval = 2·2–18·6). There was no significant sex or site difference associated with a history of previous polypectomy. These findings are consistent with the view that colorectal polyps are markers of risk (sixfold in the present study) for the subsequent development of colorectal cancer. The data also support the emerging practice that those with adenomatous polyps need regular surveillance of their large bowel as a screening measure.

Keywords: Colorectal cancer prevention, colorectal polypectomy

Adenomatous polyps of the large bowel are regarded as premalignant conditions[1–3]. This paper examines the risk of development of colorectal cancer in those who have had one or more colorectal polyps removed 12 months or longer before the onset of symptoms of their carcinoma. The data are drawn from a large population-based clinicopathological and epidemiological study of colorectal cancer, the Melbourne Colorectal Cancer Study[4]. This study has three principal arms, named the incidence study, the case control study and the survival study, and the data for this paper are drawn from the case control arm of the study.

Methods

The case control study examined the major current hypotheses of risk, causation and inhibition of colorectal cancer, namely family history of colorectal cancer, diet, alcohol, bowel habit, previous illnesses and operations (including previous colorectal polypectomy), biopsychosocial factors, parity, hormonal factors and physical activity[4]. The objective of obtaining a history of previous colorectal polypectomy was to examine the hypothesis that a history of polypectomy is a marker of risk for the subsequent development of cancer.

Definition of cases and controls

Cases constituted all histologically confirmed new cases of colorectal adenocarcinoma diagnosed in the 12 month period April 1980 to April 1981, who were usual residents of metropolitan Melbourne (population 2·81 million)[4]. Cases with a past history of ulcerative colitis or familial polyposis (10 cases) were excluded from the case control study. Community controls, who were age/sex frequency matched with the cases, were randomly selected from the same geographical area from which the cases were chosen, according to a cluster sampling plan devised by the Australian Bureau of Statistics[4]. There were 715 colorectal cancer cases and 727 age/sex frequency matched controls available for this analysis.

Data collection

Two questionnaires were administered by personal interview, each on a separate occasion by two different sets of interviewers. The first questionnaire included data on age, sex, country of birth and religion, current and past illnesses, operations (including colorectal polypectomy), medications, bowel habit, biopsychosocial factors, parity and hormonal factors and family history data. The second interview was the dietary questionnaire which included alcohol intake and tobacco consumption.

The part of the interview that dealt with previous illnesses, operations and medications was uniformly introduced by the interviewer as follows: 'Now, I'd like to talk to you about your general health. I am going to read through a list of operations. Would you tell me if you have had any of these operations and, if so, when?'. The responses were recorded as 'yes', 'no', 'don't know'. The year of the operation was also recorded. The specific question on polyps was: 'Have you had polyps in the bowel removed in the past?'. The data were not verified by any other means, such as by checking physician, pathology or hospital records. The study design was such that histopathological confirmation of the bowel polyp was not possible for the community controls. The assumption was made that 'reporting bias' and the distribution of the type of polyp would be similar for cases and for controls[4,5].

Statistical analysis of the data

The data analysis was made by unconditional logistic regressions using the GLIM statistical package[6]. Test statistics were changes in scaled deviance between nested models, these being distributed as χ^2 variables (written χ^2_n where n is the degrees of freedom (d.f.)). Cross tabulations were made using SPSSx[7].

Results

There were 715 cases (388 men and 327 women; 392 colon cancers and 323 rectal cancers), and 727 controls (398 men and 329 women). The mean age of both cases and controls was 65 years (s.d. = 10 for men and 12 for women).

There were 24 cases (10 men and 14 women) and 4 controls (2 men and 2 women) who gave a history of having had a bowel polyp removed in the past. Among the 24 cases who had a previous polypectomy, there were 16 colon cancers and 8 rectal cancers. There were 16 cases (4 men and 12 women) and no controls who did not know whether they did or did not have a bowel polyp removed in the past.

There was a statistically significant association between the history of a previous bowel polypectomy and the subsequent development of cancer ($\chi^2_1 = 17$, $P < 0{\cdot}001$, relative risk = 6·37 and 95 per cent confidence interval = 2·2–18·6). There was no significant difference between sexes ($\chi^2_1 = 0$, $P > 0{\cdot}05$). The relative risk was slightly higher in the colon cancer cases (7·2) than in the rectal cancer cases (4·5), but this difference was not statistically significant ($\chi^2_1 = 0{\cdot}8$, $P > 0{\cdot}05$). Three of the cases and none of the controls had polyps removed twice. Three of the cases had a polypectomy 1 year before the onset of symptoms, three had a polypectomy 2 years before symptoms began, two had a polypectomy 5 years before and sixteen had their polypectomy 7–30 years before the onset of colorectal cancer symptoms. Among the controls, one had a polypectomy 6 years before interview, one 15 years before and two over 20 years before interview.

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Discussion

The Melbourne data indicate that a history of a previous bowel polypectomy carries a sixfold risk for the subsequent development of colorectal cancer. There were only three cases who had a polypectomy 1 year before the onset of symptoms. This indicates that in most of the cases (21 of 24) the symptoms that resulted in a polypectomy were unlikely to be synchronous. In the only other case control study in which a history of previous colorectal polypectomy was obtained[8], 5 of 99 cases and 3 of 280 age/sex matched controls gave a past history of bowel polyps (relative risk $=4{\cdot}9$, $\chi_1^2=3{\cdot}8$, $P<0{\cdot}05$). In keeping with these present findings, Brahme and co-workers in 1974[9] reported on 123 patients who had large bowel polyps demonstrated by barium enema and subsequently removed and who were compared with 123 controls who had had normal barium enemas. At least 5 years after the initial barium enema, a repeat examination showed recurrent polyps in 26 of the polypectomy group and only in 11 of the control group ($P<0{\cdot}05$). Three colorectal cancers were discovered in the polypectomy group and none in the controls[9].

In 1974, Gilbertsen[10] reported that systematic excision of adenomatous polyps of the rectum leaving no residual rectal polyps significantly reduced the expected subsequent incidence of rectal cancer. Although this observation needs to be confirmed, the present findings do not contradict this observation, since in our Melbourne study there is only a history of a previous polypectomy and no data to indicate that the bowel was rendered polyp-free, as in Gilbertsen's series.

The authors conclude that the present findings are consistent with the current view and evidence that adenomatous polyps are markers of risk. The Melbourne data also support the view and the emerging practice that, as a screening measure, there is a need for the regular surveillance of the large bowel of those who have had adenomatous colorectal polyps demonstrated[1–3,9–11].

References

1. Morson BC. Markers for increased risk of colorectal cancer. In: Sherlock P, Morson BC, Barbara L, Veronesi V, eds. *Precancerous Lesions of the Gastrointestinal Tract*. New York: Raven Press, 1983: 255–9.
2. Sherlock P, Winawer SJ. Are there markers for the risk of colorectal cancer? *New Engl J Med* 1984; **311**: 118–9 (editorial).
3. Morson BC, Bussey HJR. Magnitude of risk for cancer in patients with colorectal adenomas. *Br J Surg* 1985; **72** (Suppl): S23–25.
4. Kune GA, Kune S. *The Melbourne Colorectal Cancer Study. A Description of the Investigation*. University of Melbourne, Department of Surgery, Repatriation General Hospital publication, 1986: 1–31. ISBN 0 86839 596X.
5. Breslow NE, Day NE. *Statistical Methods in Cancer Research. Vol. I, The Analysis of Case Control Studies*. Lyon: IARC Scientific Publications, No. 32, 1980.
6. Baker RJ, Nelder JA. *The GLIM System. Release 3*. Oxford: Numerical Algorithm Group, 1978.
7. *SPSSx User's Guide*. New York: McGraw-Hill, 1983.
8. Dales LG, Friedman GD, Ury HK, Grossman S, Williams SR. A case control study of relationships of diet and other traits to colorectal cancer in American blacks. *Am J Epidemiol* 1979; **109**: 132–44.
9. Brahme E, Ekelund G, Norden JG, Wenckert A. Metachronous colorectal polyps: comparison of development of colorectal polyps and carcinomas in persons with and without histories of polyps. *Dis Colon Rectum* 1974; **17**: 166–71.
10. Gilbertsen VA. Proctosigmoidoscopy and polypectomy in reducing the incidence of rectal cancer. *Cancer* 1974; **34**: 936–9.
11. Ekelund GR. Cancer risk with single and multiple adenomas: synchronous and metachronous tumors. In: Schottenfeld D, Sherlock P, eds. *Colorectal Cancer Prevention, Epidemiology and Screening*. New York: Raven Press, 1980: 151–5.

Paper accepted 11 June 1987

Correspondence

Ornithine decarboxylase as a marker for colorectal adenomas

Sir

I was interested to read the paper by Moorehead and colleagues (*Br J Surg* 1987; **74**: 364–5). In their discussion the authors state that the finding of diminished levels of ornithine decarboxylase in macroscopically normal rectal mucosa in patients with colorectal tumours is an unexpected finding.

No other cancers studied thus far, animal or human, have shown lower levels of ornithine decarboxylase when compared with normal tissue, as was reported in this paper. Human cancers studied thus far include astrocytomas, medulloblastomas, meningiomas, cutaneous epitheliomas, renal carcinomas, thyroid carcinomas, urinary bladder carcinomas, pancreatic cancers, gastric cancers, endometrial cancers and ovarian cancers.

Apart from the study by Rozhin, cited in the discussion of this paper, there are four other studies specifically looking at ornithine decarboxylase in colorectal cancer. LaMuraglia[1] showed a 320 per cent increase in ornithine decarboxylase in cancers and polyps and Herrera-Ornelas[2] showed an approximately two-fold increase in cancers and polyps compared with normal mucosa. In addition, LaMuraglia showed an increase in ornithine decarboxylase in non-involved mucosa taken from patients with colorectal cancer. With regard to the polyamines themselves, two studies show increased levels of polyamines in colorectal cancers compared with normal mucosa[3,4], and the study of Takenoshita shows raised levels of the polyamines in adjacent mucosa near to the colorectal cancers.

The results of Moorehead and colleagues thus conflict with all data published so far on the relationship of ornithine decarboxylase to neoplastic growth. Increased levels of ornithine decarboxylase and polyamines are required to sustain cells which exhibit an increased level of cellular proliferation.

With regard to the second paragraph of the discussion, concerning the regulation of ornithine decarboxylase activity, it should be noted that mammalian ornithine decarboxylase does not display allosteric-like kinetics and is, remarkably, not susceptible to regulatory influences of small biomolecules. Regulation of ornithine decarboxylase is at the level of translation[5].

Although a reference is cited concerning the method of ornithine decarboxylase assay, no details are given of the technique used by the authors. It was pointed out in the discussion that the warm ischaemia time may have reduced activity in tumour tissue removed, and I suspect this is the explanation for the authors' results.

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1. LaMuraglia GM, Lacaine F, Malt RA. High ornithine decarboxylase activity and polyamine levels in human colorectal neoplasia. *Ann Surg* 1986; **204**: 89–93.
2. Herrera-Ornelas L, Porta C, Pera P, Greco W, Petrelli MJ, Mittelman A. A comparison of ornithine decarboxylase and S-adenosylmethionine decarboxylase activity in human large bowel mucosa, polyps and colorectal adenocarcinoma. *J Surg Res* 1987; **42**: 56–60.
3. Takenoshita S, Matsuzaki S, Nakano G *et al.* Selective elevation of the N1 acetyl spermidine levels in human colorectal adenocarcinoma. *Cancer Res* 1984; **44**: 845–7.
4. Kingsnorth AN, Lumsden AB, Wallace HM. Polyamines in colorectal cancer. *Br J Surg* 1984; **71**: 791–4.
5. Persson L, Oredsson SM, Anehus, Heby O. Ornithine decarboxylase inhibitors increase the cellular content of the enzyme: implications for translational regulation. *Biochem Biophys Res.* 1985; **131**: 239–45.

Authors' reply

Sir

We were pleased to receive for comment the letter by Mr Kingsnorth in response to our paper on ornithine decarboxylase (ODC) as a marker for colorectal adenomas and carcinomas.

It cites four additional studies looking specifically at ODC in colorectal cancer. Two of these (La Muraglie *et al.* and Herrera-Ornelas *et al.*) were published since we wrote our paper. The other two papers deal with polyamines and colonic tumours and give no information on ornithine decarboxylase.

Contrary to Mr Kingsnorth's statement, Herrera-Ornelas and his colleagues reported no increase in ODC in cancer or polyp tissue compared with colonic mucosa from control subjects. They confirmed our finding that 'normal' mucosa from patients with tumours show significant depletion of ODC. In contrast, La Muraglia reported raised ODC levels in nearby 'normal' mucosa.

We feel that our finding of lower levels of ODC in tumours may have been affected by warm ischaemia occurring during resection, but a more major factor may have been the site of sampling. The gradient of ODC across the edge of a malignant ulcer from 'normal' mucosa requires further study.

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Colorectal cancer

Sir

We read with interest the recent paper by Toftgaard on the risk of colorectal cancer after surgery for benign peptic ulceration (*Br J Surg* 1987; **74**: 573–5) and we would like to support his finding that there appears to be no increased risk. We have recently completed both an experimental and a clinical study examining this problem. In the first study Sprague–Dawley rats ($n=72$) underwent sham operation, Polya gastrectomy or vagotomy and pyloroplasty. The colonic carcinogen azoxymethane was then administered for 6 weeks and when they were killed at 24 weeks postoperation the colons were examined for cell proliferation and tumour yield. We found that neither were increased by gastric surgery and that Polya gastrectomy actually appeared to confer some protection against tumorigenesis for reasons yet to be determined. In our clinical study we measured faecal bile acid excretion in patients who had undergone gastric surgery and we found no significant differences between them and controls. If there is an increased risk of colorectal cancer after gastric surgery for benign peptic ulcer disease[1] then it is unlikely to be due to alterations in bile acid metabolism or excretion.

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1. Bundred NJ, Whitfield BCS, Stanton E, Prescott RJ, Davies GC, Kingsnorth AN. Gastric surgery and the risk of subsequent colorectal cancer. *Br J Surg* 1985; **72**: 618–19.

Bowel preparation for colorectal surgery

Sir

It is encouraging to hear Professor Johnston base his final opinion on 'common sense' and 'hunch' (*Br J Surg* 1987; **74**: 553–4). Despite the gradual arrival of science in surgery we are still dependent upon these as the basis for most of our decisions. I would like to point to one danger in the interesting article by Irving and Scrimgeour (*Br J Surg* 1987; **74**: 580–1). Few people think that defunctioning by transverse colostomy does much to influence leakage rates. The valuable contribution of their paper is to point out that bowel preparation may similarly make little difference to leakage rates. Many of us have, however, preferred to continue the practice of defunctioning high risk anastomosis, such as those within 5–6 cm of the anal verge. We do this to minimize the mortality, and other consequences of leakage if it should occur. Irving and Scrimgeour's paper deals only with low risk anastomoses and, therefore, leaves unanswered the question of whether bowel preparation can safely be omitted from the high risk cases.

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Hormonal manipulation for pancreatic carcinoma

Sir

Mr Greenway reports optimistically on the future of hormonal manipulation for pancreatic carcinoma in his leading article (*Br J Surg* 1987; **74**: 441–2). However, this article is inaccurate in its review of the available literature. Not all of the phase II studies reported to date lend strong support for the therapeutic role of hormonal manipulation in the treatment of pancreatic carcinoma. In addition, not all of the reports demonstrating that tamoxifen does not have any therapeutic benefit are anecdotal, uncontrolled or unpublished. In 1986 we published a phase II study evaluating tamoxifen in pancreatic carcinoma[1]. Fourteen patients with unresectable carcinoma of the pancreas, which had been histologically proven at laparotomy, were entered into the study. In addition, all patients had measurable lesions, demonstrated on a CT scan. The patients were given 40 mg of tamoxifen daily and reviewed monthly in out-patients. The tumour response was objectively assessed by measuring tumour volume using CT scans every 2–3 months. No patient had a response, either partial or complete, all patients died, and the mean patient survival was 5·3 months. Therefore, in this objective study we were unable to demonstrate any therapeutic response to endocrine manipulation with tamoxifen. We also believe that it is important to point out that in both of the phase II studies detailed by Mr Greenway, to support this argument, no objective assessment of tumour response was attempted, only patient survival compared with historical controls[2,3].

Leading articles will always reflect the expert author's opinion on a given subject. However, the review of the available literature should be accurate, particularly in a highly specialized subject, so that readers can formulate their own opinions. We believe that Mr Greenway's article falls short in this requirement.

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1. Crowson MC, Dorrell A, Rolfe EB, Fielding JWL. A phase II study to evaluate tamoxifen in pancreatic adenocarcinoma. *Eur J Surg Oncol* 1986; **12**: 335–6.
2. Tonnesen K, Kamp-Jensen M. Antioestrogen therapy in pancreatic carcinoma: a preliminary report. *Eur J Surg Oncol* 1986; **12**: 69–70.
3. Theve NO, Pouselte A, Carlstrom K. Adenocarcinoma of the pancreas—a hormone sensitive tumour? A preliminary report on Nolvadex treatment. *Clin Oncol* 1983; **9**: 193–7.

Removal of retained Foley catheter

Sir

In a recent issue of the Journal, MacDermott (*Br J Surg* 1987; **74**: 25) described a method of dealing with a retained Foley catheter which had been transected: the proximal part of the catheter was pushed into the bladder by a cystoscope and, via the catheterization channel, an oesophageal varices injector was passed to puncture the balloon. A similar technique has been used routinely by us with minimal patient discomfort. A size 10–13 French gauge paediatric cytoscope (Wolf), liberally smeared with Xylocaine® jelly, was passed alongside the catheter, while the latter was put under mild traction. The balloon can be easily seen and punctured by a flexible oesophageal varices injector or the stylet of a ureteric catheter threaded down the catheterization channel. As the Foley catheter is elastic and collapsible, the adult urethra can easily accommodate a paediatric cystoscope in addition to a commonly used in-dwelling catheter.

We cannot entirely agree with the comment that dissolving the balloon with chemicals is no longer acceptable. Admittedly, a few patients experienced chemical cystitis; the incidence of bladder discomfort can be greatly reduced by filling the bladder with a maximally tolerable amount of saline before the rapid injection of a small amount of ether followed immediately by urination.

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Staphylococcal infection of open granulating wounds

Sir

The study by Marks *et al.* (*Br J Surg* 1987; **74**: 95–7) has an important microbiological component but does not acknowledge any microbiological expertise; this deficiency is reflected in the paper. Its conclusions seem to be that deep granulating wounds may become infected with *Staphylococcus aureus* but that this organism is only of clinical importance in axillary wounds, whereas it is the anaerobes that accompany *S. aureus* that delay healing in laparotomy and pilonidal wounds. Fucidin (*sic*) ointment is said to control infection in the granulating axillary wounds. However, a number of points can be raised.

There is no information on the initial bacteriology of the lesions for which surgery was performed. What were the 50 laparotomy wounds? Were some of these classed as clean contaminated or dirty operations? The wounds were first seen at varying intervals after operation, a mean interval of 23 days for laparotomy wounds for instance. Were these patients given antibiotics before they were seen in the clinic? If so, this might have some effect on the wound flora.

No details are given of the quantity of *S. aureus* isolated, or its antibiotic sensitivity. Were all strains sensitive to fusidic acid? Had any *S. aureus*, isolated after treatment, become resistant to the antibiotic?

Data on anaerobes is sparse. There is no quantitation and no details of species or their sensitivity to antibiotics—and many anaerobes are sensitive to fusidic acid. Anaerobes do not seem to have been isolated from the axillary wounds, but were the methods sufficiently sensitive for the isolation of the fastidious species commonly found?

Finally, the data suggest that these deep granulating wounds grew either *S. aureus* with or without anaerobes, or nothing. Surely this cannot be the case; were no coliforms or other species isolated? Anaerobes are frequently accompanied by coliforms or *Streptococcus milleri*.

In conclusion, we cannot accept that the data presented in this paper has shown that the wounds become infected 'from outside' with *S. aureus*, or that the axillary infection was solely staphylococcal, or that the fusidic acid ointment was necessarily treating *S. aureus*.

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Acute pancreatitis associated with carcinoma of the ampulla of Vater

Sir

We read with great interest the paper by Robertson and Imrie (*Br J Surg* 1987; **74**: 395–7) and we confirm their finding. In order to evaluate the relationship between ampullary carcinoma and pancreatic abnormalities, we have studied a series of 28 patients with proven carcinoma of the ampulla of Vater, admitted from 1978 to 1986. Among the 28 patients, 4 (14 per cent) had abdominal pain associated with hyperamylasaemia. Including these four patients, a total of eight (29 per cent) had hyperamylasaemia elevated from three to six times the upper normal level. Abdominal ultrasound examination was performed in 23 cases—13 patients (56 per cent) had a distended pancreatic duct. In all, 27 patients were operated on and a Whipple procedure was performed in 16 cases. Among these patients with pancreatic resection, histological analysis of the pancreas demonstrated that fibrosis was present in seven cases (44 per cent).

Our results indicate that biochemical, ultrasound and histological pancreatic abnormalities can be detected from 29 to 56 per cent of the time in patients with ampullary carcinoma. These pancreatic signs can be observed without clinical and/or operative findings consistent with a diagnosis of acute pancreatitis.

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Ascaris lumbricoides and intestinal perforation

Sir

We read with interest the paper by Efem (*Br J Surg* 1987; **74**: 643–4), but beg to differ. In our case, a 3-year-old girl, who had been admitted 10 months previously vomiting Ascaris worms, underwent an emergency laparotomy for intestinal obstruction. The whole small bowel was full of *A. lumbricoides* but in the terminal ileum a thickened 5 cm-long inflamed segment was found with a central perforation on the antimesenteric border, and here the worms were impacted against a competent ileocaecal valve. Analyses for typhoid, amoeba, and tubercle were negative. It is difficult, therefore, to refute the suggestion here that the worms caused an inflammatory response which led to perforation. Indeed the conditions thus created would produce a 'confined space', deemed necessary by Efem to result in perforation. We note that the new edition of Davey's work is now in accordance with our view[1].

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1. Adeloye A, ed. In: *Companion to Surgery in Africa. 2nd edn.* Edinburgh: Churchill Livingstone, 1987: 323.

Author's reply

Sir

I wish to thank Mr M. H. Cotton and Mr C. T. Faranisi for their interest and comments on my paper. However, I wish to draw their attention to the fact that they are merely repeating the errors of judgement perpetuated by previous authors, namely that *Ascaris lumbricoides* causes intestinal perforation. The new edition of Davey's *Companion to Surgery in Africa* was revised before my article was published and, therefore, the author made use of medical literature available to him. Again, the Zimbabwean surgeons did not exclude non-specific inflammation which is a common cause of intestinal pathology and perforation[1,2]. Louw 1966 stated that the normal healthy intestine of a child is capable of accommodating 5000 *A. lumbricoides* without any mechanical symptoms[3]. Impaction of a ball of ascarids occurs anywhere from the duodenum throughout the small intestine and not limited to the terminal ileum[4]. Ascarid obstruction is the commonest cause of bowel obstruction in children in Calabar but, of all the cases that I have operated upon, only a few cases of those impacted in the terminal ileum were associated with inflammatory changes. These, in late cases, could lead to bowel perforation. The question now is, was the inflammation coincidental to the presence of the ascarid ball or did the ascarid ball cause the inflammation? The former is more likely since inflammation is not commonly associated with ascarid balls impacted at other sites of the small intestine and perforations are seen in the terminal ileum where inflammatory bowel disease, including non-specific inflammations, are commonest. Mechanical pressure due to ascarid is, thus, more likely to cause pressure necrosis and consequent perforation to diseased or inflammed bowel than normal healthy bowel.

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1. Evert JA, Black BM. Primary non-specific ulcers of the small intestines. *Surgery* 1948; **23**: 185–200.
2. Dixon JM, Lumsden AB, Piris J. Small bowel perforation. *J R Coll Surg Edinb* 1985; **30**: 43–6.
3. Louw JH. Abdominal complications of Ascaris lumbricoides infestation in children. *Br J Surg* 1966; **53**: 510–21.
4. Cole GJ. Surgical manifestations of Ascaris lumbricoides in the intestine. *Br J Surg* 1965; **52**: 44–7.

Enterobius vermicularis and the appendix

Sir

I was interested in the paper by Budd and Armstrong on the role of *Enterobius vermicularis* in the aetiology of appendicitis (*Br J Surg* 1987; **74**: 748–9). I have also noted that there appears to be no relationship between *E. vermicularis* and acute appendicitis, and the observation is confirmed by a historical review of appendiceal pathology which I performed in Glasgow.

The first appendix to be submitted for pathological examination to the University Department of Pathology, Western Infirmary, Glasgow was sent in the year 1893. The table provides details of *E. vermicularis* occurrence in appendices submitted for each subsequent decade (except for 1953 when the figures are not available).

Table E. vermicularis *content of appendices in relation to year*

Year	Total number of appendices	Number containing *E. vermicularis*	Acute appendicitis plus *E. vermicularis*
1903	3	—	—
1913	144	—	—
1923	163	3	1
1933	43	1	—
1943	15	1	1
1963	626	9	3
1973	402	9	3
1983	306	8	1

Results for numbers of *E. vermicularis* occurring were identical in 1963 and 1973 and are presumably coincidental. The overall incidence of *E. vermicularis* in these 1702 appendices was 1·8 per cent. It is clear from this table that *E. vermicularis* was more commonly seen in appendices which did not show acute appendicitis.

The figures presented here would support the suggestion of Budd and Armstrong that the presence of *E. vermicularis* may be coincidental to acute appendicitis.

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Ultrasound in the diagnosis of liver metastases before surgery for large bowel cancer

Sir

The authors of a recent paper (*Br J Surg* 1987; **74**: 480–1) compare their false negative rate of 7·2 per cent favourably with that of Pain *et al.*[1] who had a false negative rate of 56 per cent only diagnosing by ultrasound 11 of 25 patients found to have metastases at operation.

In the study by Grace *et al.* 15 patients were found to have metastases by ultrasound scanning. Thirty-four patients were found to have metastases at laparotomy. This would appear to mean a false negative rate of (again) 56 per cent.

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1. Pain JA, Bailey ME, Bloomberg TJ. Liver metastases: the role of pre-operative ultrasound. *J R Coll Surg Edinb* 1984; **29**: 85–7.

Author's reply

Sir

The authors would like to thank Dr van Gelderen for his comments. The false negative rate of 7·2 per cent related to the overall population of 195 patients. Unfortunately, the authors jumped one step too far and need to eat humble pie in relation to Pain *et al*. Our false negative rate in relation to the diagnosis of metastases, as compared with metastases found at laparotomy by the surgeon, was, as Dr Van Gelderen points out, much higher than 7·2 per cent; in fact, it was 14 out of 29 (48·3 per cent). It is a moot point as to whether a suspicious ultrasound is negative or positive; I think one has to leave it in the middle and it is these patients which reduces Dr van Gelderen's 34 patients to 29.

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False aneurysm after percutaneous transluminal angioplasty

Sir

We read with interest the case report by Moran and Ruttley (*Br J Surg* 1987; **74**: 652) of the development of a false aneurysm, following percutaneous transluminal angioplasty (PTA), of an external iliac artery stenosis. On review of the first 100 PTAs for iliac artery stenoses alone, performed on 90 patients in this department, follow-up arteriography was carried out in only 6 patients. In one of these patients arteriography showed a false aneurysm. This patient was a 65-year-old woman who had a PTA of a recurrent common iliac stenosis after previous PTA and endarterectomy performed 3 and 7 years earlier, respectively. A small amount of contrast extravasation was noted on the immediate postangioplasty arteriogram. She was admitted 5 days later with buttock pain and arteriography showed a false aneurysm.

False aneurysm formation after PTA may be asymptomatic and could even protect against local restenosis. In view of this, and the low repeat arteriography rate, the actual incidence may be higher than is suggested by the current literature. Furthermore, it is likely that previous endarterectomy is a risk factor in its development.

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Management of bile duct stones

Sir

Professor Johnson deserves congratulations for his masterly review (*Br J Surg* 1987; **74**: 555–60). I would humbly point to one deficiency in his description of postexploratory check. I would agree that T tube cholangiography in the operating theatre is less than satisfactory, and that choledochoscopy markedly reduces the incidence of residual stones. There is the alternative of Foley cholangiography which is available for those of us who do not have a choledochoscope, even when we are biliary surgeons of some experience[1]. Our experience has been published[2], but perhaps reference should be made to the comparison of this method with choledochoscopy[3].

It is highly unlikely that every hospital in the UK (let alone in less fortunate countries) will be supplied with choledochoscopes. I feel the cheaper alternatives should be mentioned.

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1. Ya MT, Robinson D, Gunn AA. Per-operative cholangiography. *Br J Surg* 1973; **60**: 711–12.
2. Gunn, AA. In: *Rob and Smith Operative Surgery, 4th edn. Alimentary Tract and Abdominal Wall.* London: Butterworth, 1983: 616–36.
3. Stubs RS, Blumgart LH. Exploration of the common bile duct. *J R Coll Surg Edinb* 1984; **29**: 76–80.

Book reviews

Current Therapy in Vascular Surgery

C. B. Ernst and J. C. Stanley. 230 × 278 mm. Pp. 469. Illustrated. 1987. London: Blackwell Scientific Publications Ltd. £53.00.

This volume is edited by two acknowledged vascular surgeons from centres of some repute. They have clearly sought contributions from leading American vascular surgeons each of whom was responsible for well circumscribed topics, which in general have been ably executed. The style of presentation and the neat layout are typical of the 'Current Therapy' series. The relative paucity of illustrations is immediately obvious and renders the book a little less inviting. Illustrations help to break up the heavy uninterrupted slabs of print, which in one section reach a maximum of 49 pages. Vascular surgery is a subject which lends itself to pictorial representation and in some instances a few line diagrams, particularly of unusual operative techniques, would have enhanced the text. Notwithstanding the comments made by the editors in the preface, the lack of a reference list does not diminish the standing of the volume, which might otherwise have been regarded as a reference text on vascular surgery almost without equal. After all, contemporary thoughts and views on any vascular subject evolve from a base of expertise and knowledge amassed by previous contributions. These comments should not be allowed to detract from the overall high quality of the volume. Many authors have strengthened their papers by committing to print a searching analysis of the results of personal experience and practice in the management of a particular problem.

The liberal provision of algorithms in the management of various conditions are valuable aids to disciplined vascular surgical practice. The text contains a vast spectrum of subject matter, including cerebrovascular disease, upper extremity occlusive disease, aneurysms of the aorta and other arteries, occlusive disease affecting the lower extremity, embolism, vascular trauma, amputations, mesenteric and renal artery occlusive disease, portal hypertension, angio-access surgery, arteriovenous fistulae and malformations, and diseases of the venous and lymphatic systems. Several difficult topics, such as the effects of carotid artery surgery, vertebral artery reconstruction, fibrinolytic therapy for thrombosed grafts and penetrating trauma of the great vessels, have been commendably subjected to scrutiny. A wide range of modalities available in the management of renovascular hypertension are presented and their relative merits and demerits discussed. A fresh appraisal of conditions often ignored, such as carotid artery coils and kinking, Takayasu's disease, surgery for subclavian steal syndrome, arteriomegaly, aorto-iliac hypoplasia and iatrogenic vascular trauma, make this a comprehensive volume reflecting current practice of vascular surgery.

This book must be regarded as an invaluable and almost obligatory reference for the young vascular surgeon embarking on a future in this specialty.

A. A. B. Barros D'Sa

Gastrointestinal Emergencies

C. W. Imrie and A. R. Moossa. 158 × 240 mm. Pp. 225. Illustrated. 1987. Edinburgh: Churchill Livingstone. £25.00.

This book deals with gastrointestinal emergencies from the oesophagus to the colon. The format is clear and logical and because of this it is easily readable, but at the same time it contains enough information to serve as a reliable reference book.

The chapters on the oesophagus contain new details on the anatomy and throw light on the mechanism of bleeding from varices. The management of the bleeding is dealt with in detail, including precise information on the use of the Sengstaken–Blakemore tube—information not always included in text books.

There are important messages in the chapter on bleeding from peptic ulcers, the first rather depressingly states that endoscopic diagnosis has not altered the outcome in upper GI bleeding when heterogeneous groups of patients are studied. Endoscopy is important, however, in identifying the small sub-group of patients with a visible vessel in the base of the ulcer who are at a high risk of re-bleeding.

It is particularly useful to have the latest facts on acute pancreatitis under one cover. The prognostic indices are evaluated and the latest ideas in treatment are included.

There were a few omissions, for example the chapter on colonic emergencies and abdominal trauma did not deal with the management of perforating injuries of the colon. This can present problems for the inexperienced surgeon and is worth dealing with in some detail. In conclusion this is a useful, compact reference book.

J. M. Kelly

Intestinal Obstruction. Volume 13

L. P. Fielding and J. Welch. 250 × 190 mm. Pp. 177. Illustrated. 1987. Edinburgh: Churchill Livingstone. £30.00.

This book on intestinal obstruction is volume 13 of the series *Clinical Surgery International*. The first six of the fourteen chapters set out to describe the basic science aspects of obstruction, and start off with excellent accounts of the relevant embryology and surgical anatomy which are well illustrated. However, this is a multi-author work and only the first two chapters are written by the same contributors. The account of the pathophysiological effects of obstruction is most instructive but this section of the book then rather loses its way, and one gets the impression that at least one pair of authors were allocated a subject which ran dry.

The remaining section of the book deals with the clinical and operative management of obstruction but gets off to an awkward start. The injunction never to attempt the reduction of an incarcerated hernia, and the ready recourse to Swan–Ganz catheters and digitalization, make one wonder if the complicated formulae to correct acid–base balance are founded on common sense. However, the balance is subsequently redressed by a fund of ideas and alternatives. The case for ultrasound examination of the bowel wall where viability is doubtful is persuasively argued. The chapter on radiology is disappointing since, having dwelt over-long on the stomach, it relies heavily on contrast studies of the small bowel.

The management of large bowel obstruction is covered by two chapters and the first is as pedestrian as the second is exciting. The safe 3-stage procedure for the ordinary surgeon is still with us, but the St. Mary's study and primary anastomosis after on-table lavage get a good hearing. Two useful contributions, on pseudo-obstruction and postoperative ileus, complete this comprehensive account of intestinal obstruction.

This is not a book for the current Fellowship candidate but at least half of the chapters are enjoyable and informative reading.

T. Bates

Atlas of General Surgery. Second edition

H. A. F. Dudley, D. C. Carter and R. C. G. Russell. 276 × 219 mm. Pp. 1002. Illustrated. 1986. London: Butterworths. £39.50.

As the Editors state, nearly all the material in *Atlas of General Surgery* is culled from Rob and Smith's *Operative Surgery*. The fact that after 5 years it has needed a second edition is a testimonial to its success. This is an extract from the larger encyclopaedic volumes of those operations of more immediate practical interest to the general surgeon. Thus, it includes chapters on wounds, access to the chest for the lungs and the heart, all the gastrointestinal tract, the urinary tract, some relevant aspects of neurosurgery, the essentials of vascular surgery including varicose veins, basic endocrinology, and the breast.

It has all the qualities of the parent work with clear and plentiful illustrations and appropriate text; different techniques are discussed but generally the text is rightly confined to technical operative details. However, in some chapters the introductory text could be pruned ('Laparotomy for intestinal obstruction', 'Intestinal anastomosis', 'Cholecystectomy', 'Portal hypertension and porto-caval anastomosis', and chapters on hernias and varicose veins). There is also some unnecessary reduplication (anastomosis by stapling is discussed identically in five different chapters—'End to end anastomosis using circular stapling device', 'Staplers', 'Elective operation for sigmoid diverticular disease', 'Anterior resection' and 'Hartmann's operation').

Unchallenged results of personal series are totally uncalled for in such a work ('Porto-caval anastomosis' and chapters on hernias). The best chapters, and they are the majority, have a very short introduction, clear drawings and helpful explanatory text with a few comments on postoperative care and complications. The readers of this text will already have decided to perform a particular operation and are essentially interested in technical details and not in a small treatise of symptomatology and results.

The table of contents and the index are helpful, and the cost reasonable. Altogether, this is a very good book which amply fulfils its objective. With some trimming and deletions it would be excellent. Those operating theatres who do not have the complete *Operative Surgery* must at least have *Atlas on General Surgery* on their shelves in the operating theatre suite. Every operation described is a must for the English FRCS examination.

G. Jantet

Renal Transplantation

M. R. Garovoy and R. D. Guttmann. 242 × 168 mm. Pp. 446. Illustrated. 1986. Edinburgh: Churchill Livingstone. £47.50.

I enjoyed reading this book. The fact that the Editors work in California and Montreal is heavily reflected in the choice of authors—most of whom are based in North America and the only exception worked for a considerable time in North America. The book is a little more than 400 pages long and is a pretty comprehensive attempt to cover the field of renal transplantation, dealing with important topics from dialysis right through to rehabilitation and pregnancy in transplant recipients. There is a very good chapter on paediatric transplantation.

Although the overall standard of the book is good, a number of criticisms can be made. For example, there is no real excuse for printing a graph showing graft survival which was published in 1977. So much has changed in 10 years that a more modern set of figures would have been appropriate. I encountered this old graph early on and soon after there was a statement saying that dialysis was the preferred treatment for renal failure and that transplantation should be regarded as 'a holiday from dialysis'. I doubt that this statement would find any sympathy amongst transplant surgeons nowadays. There are a number of other anachronisms; for example, it is stated that barium meal should be performed for patients suspected of having duodenal ulceration. Surely nowadays the preferred investigation is endoscopy? I was also interested to note that the quoted figure for CAPD in the United States is 5–10 per cent, I suspect that this figure is a considerable underestimate in 1987. However, after rather an indifferent start the book produced very few irritations in its middle part. There were a few rather unnecessary misprints but I did not take great exception to anything until nearly the end of the book, where it was stated that diabetics were excluded from transplantation in Great Britain because of the belief that satisfactory rehabilitation was unobtainable. In the authors' defence a British reference is quoted to support this statement, but the reference is 4 years out of date and I am not sure that the statement was even right 4 years ago, and certainly is wrong now. In the chapter on the technicalities of surgery it was suggested that endarterectomy should be performed on an occluded internal iliac artery before anastomosing the renal artery to it. Again, I doubt if this is practised in Britain and I personally believe that it is a very poor surgical method.

The criticisms I have made are of detail only and they do not really affect the overall impression created by the book. It is an excellent publication for those who wish to have a reasonably up-to-date overview of the current situation in renal transplantation, and to have that overview contained within one book rather than a series of disconnected articles. It can be recommended for those who are anxious to acquire a more extensive knowledge of renal transplantation. It can even be recommended for those who believe they already know a great deal about the subject; they might learn something from it and if they do not the literature cited is very extensive and, for the most part, reasonably up to date.

R. M. R. Taylor

A Colour Atlas of Mastectomy with Immediate Reconstruction

D. J. T. Webster. 265 × 195 mm. Pp. 63. Illustrated. 1986. London. Wolfe Medical Publications Ltd. £17.00.

This addition to the Wolfe 'Single Surgical Procedures' series is clearly and comprehensively illustrated. The number and quality of the colour plates are such that the book will be most useful to the trainee and the established surgeon who are coming newly to the techniques described. The text has two components. The first is a thoughtfully introduced and carefully described method of performing the Patey modified radical mastectomy, with a short addendum extending the description to embrace Halsted radical mastectomy. In the course of this section Mr Webster weaves into his description a number of small but valuable tips which emanate from the large personal experience which he and his Cardiff colleagues have of performing this operation. The second section of this atlas deals with reconstruction of the breast. This opens with an incisive discussion about selecting the optimum technique for breast reconstruction in the individual patient. Techniques described range from the immediate insertion of a 'permanent' prosthesis, through tissue expansion and latissimus dorsiflaps, to the use of the rectus abdominis muscle for reconstruction of the breast.

Inevitably there are minor differences of detail and emphasis about which the individual reader will disagree with the author. However, overall, this readable text liberally studded with gems of valuable advice will be a great asset to surgeons of all grades who manage patients with cancer of the breast.

P. E. Preece

Progress in Surgery. Volume 2.

I. Taylor. 155 × 233 mm. Pp. 245. Illustrated. 1987. Edinburgh: Churchill Livingstone. £15.00.

This is the second volume entitled *Progress in Surgery* edited by Professor I. Taylor. Its purpose is to review surgical conditions in which there has been recent progress in understanding and management. A total of 15 chapters review 4 specialist and 11 general surgical topics; the standard of review is high.

The four specialist subjects reviewed include prognostic factors in cancer of the head and neck, basic management of neonatal surgical emergencies, an interesting chapter on advances in the treatment and diagnosis of brain tumours and an authoritative and clearly written account of the management of patients with transient ischaemic attacks by means of carotid endarterectomy (although the precise role of operation in the treatment of this condition remains uncertain).

The histology, pathophysiology and management of constipation and incontinence in relation to anorectal function are clearly presented in an informative and practical chapter. Surgeons will also find a clear exposition of the causes, pathology, pathophysiology and treatment of radiation damage to the bowel in a comprehensive and eminently readable chapter on this subject. Other chapters review the diverse subjects of management of stones in the common bile duct, staging and management of gastric cancer, the management of liver metastases and progress in tumour biology.

Current surgical reviews are overviewed in chapters on parenteral nutrition, gastro-oesophageal reflux, the role of surgery in pancreatitis, the management of lower gastrointestinal haemorrhage and adjuvant systemic chemotherapy of the breast. In general, these chapters give excellent reviews with good historical background data, informed discussion of controversial views and sound advice on resultant surgical practice. In many subjects, 'progress' may be debatable, but this book is a valuable source of well presented, up-to-date information and references. At £15.00 it is recommended to surgeons of all grades.

A. Gunn

Burns and their Treatment. Third edition.

I. F. K. Muir, T. L. Barclay and J. A. D. Settle. 168 × 240 mm. Pp. 178. Illustrated. 1987. London: Butterworths. £25.00.

John Settle, Clinic Physiologist and Director of the Yorkshire Regional Burns Centre has joined the two original authors in the third edition of this account of burns and their management. The pathophysiology of burns is clearly described, including the rationale of varying replacement fluid regimens which might be required. The reader is, thus, able to formulate management profiles according to the needs of the patient, and is encouraged by the authors to retain flexibility and frequent assessment of the burnt patient. There is a summary where appropriate at the end of each chapter for quick reference. The book is well illustrated and subheadings are placed at the top of each page. General care of the burnt patient is emphasized as are the difficult problems associated with sepsis. The book contains accounts of burns of special areas, varying types of burns, the management of scars and contractures and the administrative aspects of a burns unit. This concise study of burns and their treatment is a satisfactory blend of clinical sense and applied physiology. It will prove invaluable to all grades of surgeon engaged in the treatment of burns and is a handy volume to keep in the casualty department and intensive care units of district general hospitals.

M. Crumplin

Scientific Basis of Urology

A. R. Mundy. 250 × 190 mm. Pp. 409. Illustrated. 1987. Edinburgh: Churchill Livingstone. £60.00.

Newcomers to the speciality of urology could do worse than begin with this book if only for its lucid review of ureteric physiology and the stimulating account of acute and chronic renal failure. Elsewhere, the standard is not uniform: the account of fertility and potency has been overtaken by Brindley's research and, curiously enough, continues to advocate varicocolectomy without acknowledging the controlled studies which refute it. The account of imaging is useful but leaves out nuclear magnetic resonance and, alas, the reader who wants to find out the embryological explanation for most of the congenital anomalies will continue to look in vain. Nevertheless, this book will be very helpful to senior registrars embarking on specialist training; their chiefs will find this a most valuable review of a literature which grows at a staggering rate.

J. Blandy

Notices and announcements

6 November 1987
Colonoscopy Teaching Day for Beginners
Southampton, UK
Information: Peter McDonald, Lecturer in Surgery, Department of Surgery, F Level Centre Block, Southampton General Hospital, Tremona Road, Southampton SO1 6HU, UK

6 November 1987
12th Annual Meeting of the Pancreatic Society of Great Britain and Ireland
London, UK
Information: Mr C. W. Imrie, Consultant Surgeon, Royal Infirmary, Glasgow G4 0SF, UK

11–13 November 1987
First International Congress in Oral Cancer
Singapore
Information: Dr N. Ravindranathan, The Secretariat Department of Oral Surgery, Faculty of Dentistry, National University of Singapore, Kent Ridge, Singapore

12–14 November 1987
Seventh Annual William Beaumont Army Medical Center Trauma Symposium: Controversies in Head and Neck Trauma
El Paso, Texas, USA
Information: LtC Troy M. Reyna, MD, Chief, Trauma Service, William Beaumont Army Medical Center, El Paso, Texas 79920-5001, USA

13–15 November 1987
14th Annual Symposium on Current Critical Problems and New Horizons in Vascular Surgery
New York, USA
Information: Continuing Medical Education, Albert Einstein College of Medicine, Montefiore Medical Center, 3301 Bainbridge Avenue, Bronx, New York 10467, USA

15–18 November 1987
All Americas Health '87
Tampa, Florida, USA
Information: Denis Beckett, Fairs and Exhibition Ltd, 51 Doughty Street, Gray's Inn, London WC1N 2LB, UK

16–20 November 1987
Fourth International Symposium on Cardiorespiratory Emergencies
Rotterdam, The Netherlands
Information: Dr Omar Prakash, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands

1–2 December 1987
First International Symposium on Aids and the Surgeon
London, UK
Information: Ms Pauline Sleight, BDI Conferences Ltd, Kensington Business Centre, 9–11 Kensington High Street, London, W8 5NP, UK

19–21 December 1987
2nd International Surgical Congress and Workshop on 'Surgical Manpower and Technology—Development and Utilization in Developing Countries'
Dhaka, Bangladesh
Information. Professor Golam Rasul, Department of Surgery, Institute of Post-Graduate Medicine and Research, Shahbag, Dhaka, Bangladesh.

23–24 January 1988
Hong Kong Surgical Forum Winter 1988
Hong Kong
Information: Forum Secretary, Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong

4–9 February 1988
54th Annual Meeting of the American Academy of Orthopaedic Surgeons
Atlanta, USA
Information: Lois Stratmeier, 444 North Michigan Avenue, Suite 1500, Chicago, Illinois 60611-3981, USA

8–12 February 1988
Third Biennial Conference of the Indian Society of Oncology and the Indo–USSR International Workshop on Oesophageal Cancer
Bangalore, India
Information: Conference Secretariat: Kidwai Memorial Institute of Oncology, Hosur Road, Bangalore-560 029-India

13–15 April 1988
Annual Meeting of the Association of Surgeons of Great Britain and Ireland
Harrogate, UK
Information: Mr B. T. Jackson,, The Royal College of Surgeons of England, 35/43 Lincoln's Inn Fields, London WC2A 3PN, UK

1–6 May 1988
Bicentennial Scientific Meeting Royal Australasian College of Surgeons
Brisbane, Australia
Information: 1988 GSM, Royal Australasian College of Surgeons, Spring Street, Melbourne, Australia 3000

5–7 May 1988
Biennial Congress of the European Council of Coloproctology 1988
Geneva, Switzerland
Information: General Secretary of the European Council of Coloproctology, Policlinique de Chirurgie, Hôpital Cantonal Universitaire de Genève, 1211 Geneva 4, Switzerland

8–11 May 1988
Joint Annual Meeting of the American Lung Association, the American Thoracic Society and the Congress of Lung Association Staff
Las Vegas, USA
Information: Deborah Richardt, American Lung Association, 1740 Broadway, New York 10019, USA

12–14 May 1988
Second Vienna Shock Forum
Vienna, Austria
Information: AUSTROPA Kongbressbüro, Friedrichstrasse 7, A-1010 Vienna, Austria

22–28 May 1988
VII Iberolatinamerican Congress of Plastic Surgery
Cartagena, Colombia
Information: Sociedad Colombiana De Cirugia Plástica, Ap. Aéreo Nos 6658; 6572, Bogotá DE, Colombia, South America

29 May–3 June 1988
Second World Congress on Hepato-Pancreato-Biliary Surgery
Amsterdam, The Netherlands
Information: Q. A. Laman Trip, Organizer, Alton House, Keizersgracht 792, 1017 EC Amsterdam, The Netherlands

12–17 June 1988
Cardiovascular and Interventional Radiological Society of Europe
Berlin, FRG
Information: Dr Reingard Sörensen, Klinikum Steglitz, Röntgendiagnostik, Hindenburgdamm 30, 1000 Berin 45, FRG

20–22 June 1988
7th International Workshop for the Study of Vascular Anomalies
Hamburg, Germany
Information: Dr John B. Mulliken, The Children's Hospital, 300 Longwood Avenue, Boston MA 02115, USA

29 June–1 July 1988
International Symposium on Therapeutic Progress in Urological Cancers
Paris, France
Information: Dr Saad Khoury, Clinique Urologique (Pr Chatelain), Hôpital de la Pitié, 83 Bd de l'Hôpital, 75634 Paris, Cedex 13, France

3–9 July 1988
16th World Congress of the International College of Surgeons
Milan, Italy
Information: Secretariat, Clinica Chirurgica III—Università degli Studi, Via F Sforza 35, 20122 Milan, Italy

9–10 July 1988
Hong Kong Surgical Forum Summer 1988
Hong Kong
Information: Forum Secretary, Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong

11–19 September 1988
XIIth International Congress of the Transplantation Society of Australia and New Zealand
Sydney, Australia
Information: Dr B. Hall, Honorary Secretary, Transplantation Society of Australia and New Zealand, 145 Macquaire St, Sydney 2000, Australia

ROB AND SMITH'S OPERATIVE SURGERY · FOURTH EDITION

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Hugh Dudley, ChM, FRCS(Ed), FRACS, FRCS. Professor of Surgery, St Mary's Hospital, London, UK.

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R C G Russell, MS, FRCS. Consultant Surgeon, Middlesex Hospital, St John's Hospital for Diseases of the Skin and Royal National Nose, Throat and Ear Hospital, London, UK.

Plastic Surgery Fourth Edition

Edited by
T L Barclay ChM, FRCS, FRCS(Ed). Formerly Consultant Plastic Surgeon, Bradford Royal Infirmary and St Luke's Hospital, Bradford, UK.

Desmond A Kernahan MD, FRCS(C), FACS, Chief, Division of Plastic Surgery, Children's Memorial Hospital, Chicago, Illinois, Professor of Surgery, Northwestern University Medical School, Chicago, Illinois, USA.

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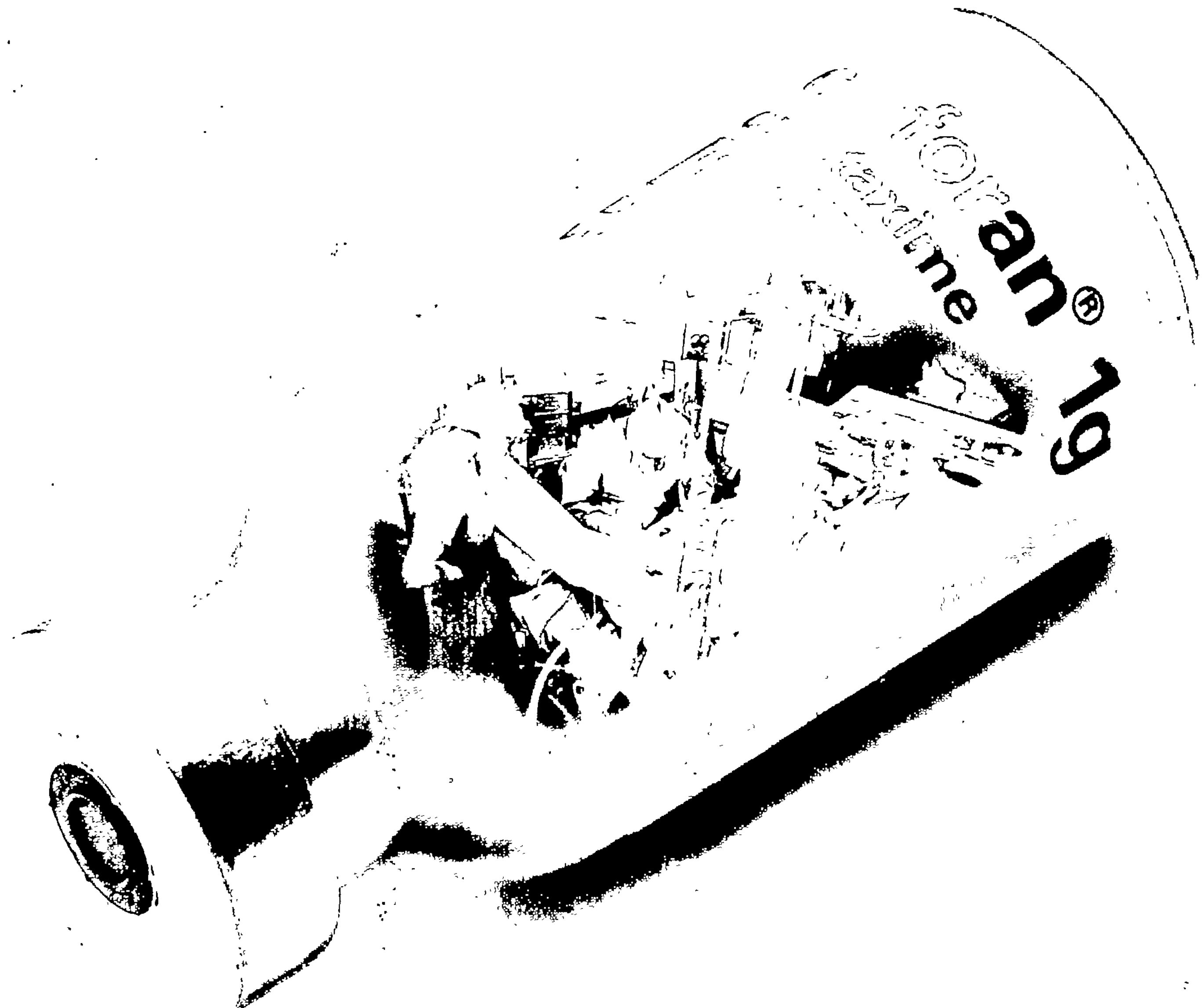

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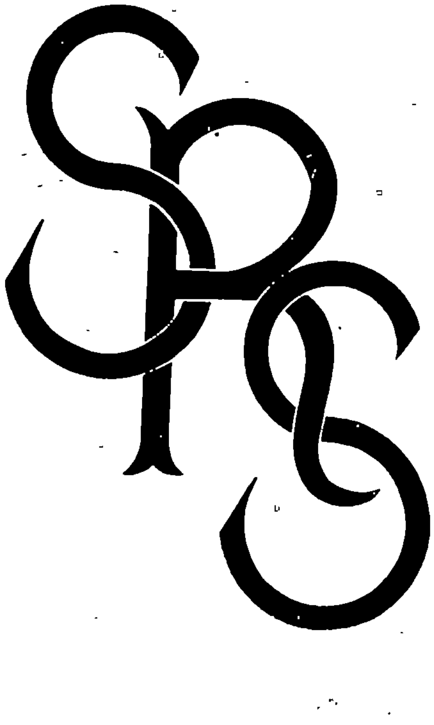
The British Journal of Surgery

Volume 74, Number 12, December 1987



BOOKS FROM BUTTERWORTHS

ATLAS OF GENERAL SURGERY • Second Edition

Hugh Dudley ChM, FRCS(Ed), FRACS, FRCS
Professor of Surgery, St Mary's Hospital, London, UK

David C Carter MD, FRCS(Ed), FRCS (Glas) St Mungo Professor of Surgery, University of Glasgow; Honorary Consultant Surgeon, Royal Infirmary, Glasgow, UK

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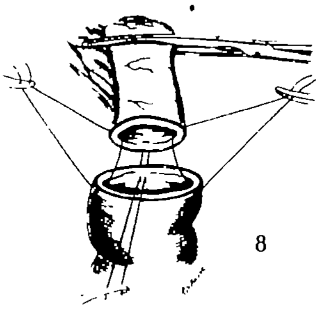

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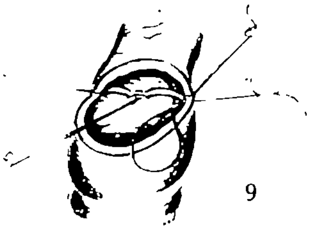
This comprehensive, one-volume atlas presents detailed accounts of virtually all the operations likely to be required in general surgical practice. Leading surgeons from around the world describe their techniques for performing the operations safely and successfully, giving precise, step-by-step details, and discussing pre-and post-operative surgery relevant to effective practice. Every aspect of each procedure is meticulously illustrated with specially commissioned surgical drawings.



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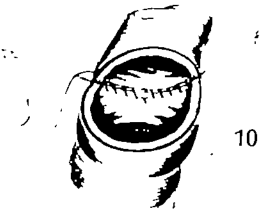
Virtually all the material has been previously published in the fourth edition of the authoritative Operative Surgery Series, but for this new edition of the Atlas, chapters on intestinal stapling have been included. The selection of topics has been carefully re-assessed with the needs of the general surgeon in mind, and there is now much greater emphasis on abdominal and vascular procedures.



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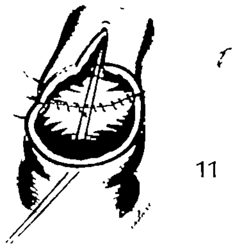
Now over 1000 pages long and containing almost 100 chapters, the second edition of the *Atlas of General Surgery* will remain *the* indispensable reference for both experienced surgeons and those in training.



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Reviews of previous edition

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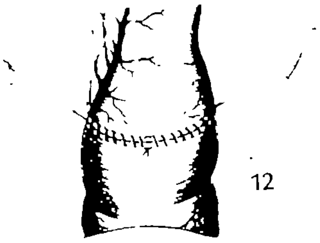

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References

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Surgical research: is it important for training?

Changes in general surgical training in the UK seem inevitable. Alterations in the FRCS regulations and manpower manipulations, as envisaged by the Joint Planning Advisory Committee, of both registrar and senior registrar numbers are occurring at a time when condensation, from a roughly 12–14-year postgraduate training programme to one of 10–12 years, is the primary aim with numerical equalization of 'career' registrars and senior registrars. This change could in part be achieved by elimination, in all but a few instances, of a period of surgical research from the training programme.

Throughout the 1980s a period of research activity culminating in a higher degree by thesis examination has been a prerequisite for progress on the surgical ladder to senior registrar and consultant appointments. There can be little doubt that 'market forces' have been a prime motivation for the initiation and expansion of research activity. As a result, the majority of surgeons at some period during their training have contributed to surgical science. This can best be illustrated by analysis of applications for senior registrar posts. A survey from the Wessex region is probably fairly typical of the situation nationwide[1]. For a senior registrar post in 1985 there were 66 applicants of whom 8 were short-listed. Their mean age was 33·5 years, corresponding to a mean age of acquiring a consultant post of about 38 years. They had completed at least 3 years as a post-FRCS clinical registrar; 86 per cent of applicants had spent a mean of 1·8 ± 0·5 years in full-time research whereas all short-listed candidates had been in full time research (mean 1·9 ± 0·2 years). Half of the applicants had obtained, submitted or written a thesis. Short-listed candidates had published an average of seven papers and presented about ten. Other aspects which illustrate this level of research activity are the steady appearance of new surgical journals containing research papers, and the increasing numbers of abstracts submitted for consideration to surgical societies; over 600 abstracts are submitted per year to the Surgical Research Society alone.

How important is surgical research to the overall training of a general surgeon? If it is to be regarded as 'essential', irrespective of 'market forces', then it should be available to all and this should be reflected in surgical training programmes. If it is to be regarded as an 'optional extra' then its importance as a discriminator of merit and ability will be diminished. However, if a period of surgical research cannot be shown to provide tangible benefits then perhaps it should be available only to those who wish to pursue an academic career.

Surgical research can vary in its clinical and scientific balance and in the extent of direct involvement in design, measurement and analysis. Much variety also exists in the collaborative links and supportive research strategies within institutions and departments. Within academic departments of surgery much of the research effort at levels below the direction of broad strategy is borne by research registrars. Most of the departmental staff are clinicians with relatively short tenure. Only those of consultant status stay for more than about 4 years, research fellows stay for nearer 2 years; the number of basic scientists is relatively low.

At the very least it should be possible to influence the choice of research projects being utilized within the current system, if a particular format can be shown to give superior results. More radically, it is possible to suggest changes in the structure of higher degrees, perhaps as proposed in one form by Calne[2], by differentiating between surgeons aiming in some measure at an academic career and those bent on more exclusively clinical careers. Beyond this one might propose courses outside the single project degree system, perhaps involving elements such as assessment of research and personnel or financial management experience.

The case against higher degrees as an effective research strategy is fairly obvious. Few research registrars are active in laboratory research for much more than 2 years. Their effort during this time is directed firstly at attuning themselves to an alien working environment, then to solving specific problems within the confines of their chosen project; work may lack depth of perspective. The requirements of thesis production are of prime importance. Intradepartmental scientific support is often limited in the scope or range of disciplines, much work is done externally and the

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cumulative departmental experience is retarded. In the system's favour is that the predominance of research workers with primarily surgical ambition keeps the field practically focused. The tight time schedules are advantageous in promoting productivity. Supplies of fresh ideas are not a problem and the interchange between the working body of a profession and its academic arm is intrinsically attractive. Finally, the satisfaction and sense of achievement in obtaining an MS (or equivalent) should not be understated.

To investigate this area would involve determining the fate of thesis work in terms of full publication and citation indices within and between fields of study. It might be possible to compare surgeons with other professionals seconded into research work, perhaps in engineering. It would also be worth investigating the origins of recent advances in surgical practice to evaluate the role of research experience.

Modern argument insists upon demonstrating 'cost-effectiveness' in most strategies. Manpower difficulties, changes in attitudes towards training, and novel qualifying examinations all necessitate a re-evaluation of surgical training objectives. It is becoming increasingly important to provide 'hard' data to support these broad strategies, particularly with regard to research activity. If surgical research endeavour is important, and firm evidence is provided to support this, then it should be integrated into surgical training programmes in such a way that manpower constraints are effectively considered. The acquisition of a higher degree by thesis examination under these circumstances would be irrelevant since the completion of training would signify the automatic inclusion of research activity.

Programmes which acknowledge this integrated approach to training are possible. In Wessex, for example, we have a 3-year 'middle grade' rotational training scheme (a possible prototype for a 'career' registrar rotation). The first year is spent in clinical work in a district general hospital, but allows one full day for research in the University department. During this year the basic concepts and methodological aspects of research are dealt with. The second year involves full-time research but with some minor clinical commitment. The third year is spent in a different district general hospital and the 1 day per week release is utilized to enable completion of studies and 'writing up'. In addition to this training programme, we have introduced over the last 3 years a laboratory course for registrars, designed specifically to enable them to become familiar with research methodology and techniques.

Finally, if the new FRCS regulations require an assessment during the period of higher surgical training, does this necessarily need to be a conventional examination? If research activity is considered to be of benefit why not rely upon the submission of a dissertation encompassing original research in the particular specialty which the individual has pursued during his career?

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1. Taylor I, Clyne CAC. Senior Registrar applications in general surgery in 1982 and 1985. *Br Med J* 1985; **291**: 143–4.
2. Calne RY. Surgical research—curiosity and luck: personal observation and prejudices. *Ann R Coll Surg Engl* 1984; **66**: 211–13.

Confidential Enquiry into Perioperative Deaths

This month has seen the publication of this important study established by the Associations of Surgeons and of Anaesthetists of Great Britain and Ireland, and supported by Nuffield Provincial Hospitals Trust and King Edward's Hospital Fund for London. Perioperative deaths (4034) in three English regions over a 12-month period (485 850 operations) form the basis of the study. Accepting the difficulties inherent in such studies, four sets of recommendations are made. Standards must be assessed nationally with adequate data collection and audit, coupled with regular self-assessment by clinicians. Consultant anaesthetists and surgeons must ensure supervision of trainees. The decision to operate on the elderly and very sick should be made at consultant or senior registrar level and the difficulty of making a decision not to operate is emphasized. Finally, organizational issues are addressed emphasizing that few operations need to be performed at night and that operations should only be performed by surgeons with adequate training in the relevant speciality. While these recommendations contain little that is surprising, this report will provide an invaluable basis for future planning.

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The role of non-invasive tests in arterial disease

Inventive use of Doppler ultrasound and other non-invasive methods has provided the foundation and fabric of the modern vascular laboratory. However, the sceptic might reasonably question the impact of these techniques on clinical decisions and ask how many tests, now routine in some laboratories, influence patient management. Many vascular surgeons seem to manage patients well using little more than clinical examination and arteriography, while others receive a detailed vascular laboratory report before they meet the patient.

Non-invasive tests can offer haemodynamic information which arteriography does not, and they may eventually replace arteriograms in many situations. At present they have three main roles: helping with the decision to proceed to arteriography; supplementing arteriography with more precise information about blood flow and plaque morphology and following up the results of vascular reconstruction. An additional and more contentious area is the assessment of asymptomatic disease.

We can begin by examining the investigations that might helpfully precede arteriography. In the lower limbs, ankle pressure measurements using the Doppler probe give objective and repeatable data on the severity of ischaemia, and a progressive decrease in ankle systolic pressure may weight the decision to operate[1]. When used with an exercise test the presence of arterial disease can be confirmed or excluded in doubtful cases. Unfortunately, calcification may make the vessels partially or wholly incompressible and spuriously high readings (notably in diabetics) may reassure the inexperienced. The measurement of toe pressures overcomes this problem since the vessels are rarely calcified, but this investigation is technically more difficult and has its own inaccuracies.

Assessment of the aorto-iliac segment remains a difficult and important problem in some patients since arteriography may not demonstrate stenoses adequately. Analysis of Doppler waveforms from the common femoral artery, and thigh pressure or pulse wave recordings have all been advocated[2], but none seems universally satisfactory[3]. Measurement of femoral artery pressure after vasodilatation is perhaps the best method of all but this is invasive[4].

In the legs, therefore, assessment by ankle pressure measurement is simple and helpful and can be done with a hand-held Doppler in out-patients. Other techniques, while giving guidance in some difficult cases, do not in general influence decisions. Assessment of the smaller vessels in the limbs by techniques such as transcutaneous oxygen measurement, laser Doppler, and radioisotope clearance are useful research tools but, as yet, are not of proven value in making decisions about surgical reconstruction.

The other major area in which the non-invasive vascular laboratory plays a part is the assessment of carotid disease, and here the duplex scanner (real time ultrasound plus Doppler) has emerged as an important and powerful tool which is ideally suited to detailed analysis of selected small areas within the blood vessels[5]. It has largely replaced indirect techniques such as periorbital Doppler studies and oculopneumoplethysmography, although these can still be useful for assessing collateral blood supply to the brain when the internal carotid arteries are severely stenosed. The duplex scanner has also superseded the Doppler scanner because it enables detailed assessment of stenoses and plaque morphology as well as flow. Considerable skill is required to use this expensive machine well but, where this is available, some surgeons are now prepared to perform carotid endarterectomy on the evidence provided by duplex scanning alone.

The duplex scanner must rank as the most significant technical development in non-invasive vascular assessment to have emerged in recent years. Using lower frequencies of ultrasound it can be used to examine deep seated vessels such as the renal[6], coeliac, and mesenteric arteries[7] and can be used to compute blood flow (in millilitres per min) in any artery which can be satisfactorily imaged. In addition to pre-operative evaluation, it can be used intra-operatively to detect technical defects[8], and postoperatively to image grafts and measure flow along them[9]. This method of follow-up is more sensitive than ankle pressure measurement in diagnosing graft stenosis.

The use of extensive and expensive non-invasive measurements on all patients with arterial disease has proved unnecessary and, using a whole battery of vascular

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laboratory tests as routine screening, before clinical assessment by the vascular surgeon, wastes both time and money. But the judicious use of specific investigations can greatly enhance our knowledge of haemodynamic disturbances and improve our management of patients. In the lower limbs, ankle pressure measurement after exercise can reduce the number of patients requiring diagnostic arteriography, and duplex assessment of carotids has reduced the necessity for potentially hazardous carotid arteriography. Digital subtraction angiography has less hazards than conventional studies but still poses certain risks and discomfort for the patient. The ability to diagnose and treat graft stenoses early on, before occlusion, should diminish the need both for replacement grafting and for amputation in some patients[10].

For the busy vascular surgeon a hand held Doppler still provides the most important and essential non-invasive tool, with a treadmill as a useful adjunct. Where resources and technical assistance permit, a duplex scanner offers the most helpful and versatile addition to his diagnostic armamentarium, although its cost effectiveness for every district general hospital has still to be proved.

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10. Wolfe JHN, Lea Thomas M, Jamieson CW, Browse NL, Burnand KG, Rutt DL. Early diagnosis of femorodistal graft stenoses. *Br J Surg* 1987; **74**: 268–70.

Review

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Vascular trauma

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Civilian vascular trauma is not uncommon. Prompt treatment with modern vascular surgical techniques produces good results.

The escalating incidence of terrorist violence in Western Europe and the experience in Northern Ireland have increased awareness of the problems of major vascular trauma complicating limb injuries. All surgeons admitting accident cases should understand the modes of presentation of vascular trauma and be able to initiate a management plan which will maximize the chances of limb salvage.

Throughout the Second World War arterial trauma was managed by ligation, with an overall amputation rate of 40 per cent[1]. In the Korean and Vietnam wars a remarkable reduction in limb loss was achieved by pursuing a policy of vascular reconstruction[2,3]. Many of the lessons learnt in these major conflicts have been translated into civilian practice[4–6]. Young, previously fit, adults are the group most at risk of sustaining vascular trauma. They are likely to survive the injury but have the most to lose in terms of quality of life if surgical treatment is unsuccessful[7–9].

Injury to vessels can be a consequence of penetrating and blunt trauma. In the USA most penetrating vascular trauma is caused by firearms whereas in the UK these injuries are usually the result of stabbing[10–16]. Blunt trauma sufficient to cause disruption of major vessels occurs in road traffic accidents and in serious crush injuries (in the engineering and construction industries)[17,18]. Iatrogenic arterial injury is increasing, in particular damage to the brachial artery following catheterization for coronary angiography[10,11,17].

Pathophysiology of vessel injury

Penetrating injuries can lacerate or transect the arterial wall; transection may result in spasm with some control of blood loss[11]. Laceration damage is usually limited to the precise site of trauma. Similar lesions are caused by low velocity hand guns where damage is limited to the 2–3 mm surrounding the track of the bullet[9,19]. Penetrating trauma inflicted by explosive debris, shotgun or high-velocity missiles causes more widespread tissue destruction[5,19] with significant loss of arterial wall[12]. The cavitation effect produced by high-velocity missiles causes tissue destruction well away from the initial visible damage[3]. The most devastating injuries are those sustained from a shotgun fired at close range[4].

Blunt injuries can cause a variety of stresses on the vessel wall due to lateral displacement or stretching, often with obvious disruption. Alternatively, while the external surface of the vessel appears relatively unaffected, the lumen may be occluded by internal damage producing an intimal flap[11,17,20]. Signs of thrombosis in vessels damaged by blunt injury or high-velocity missile trauma may occur at a variable time after the injury as platelet aggregates form[21,22].

Arterial spasm is a well-recognized consequence of minor vessel trauma. However, identical symptoms and signs can occur when spasm is accompanied by intimal damage and the diagnosis of spasm should only be considered at operation[12,21,23–25].

Up to 17 per cent of vascular injuries may present late with either an arteriovenous (A–V) fistula or an aneurysm[5,15,18]. The injury which subsequently results in an A–V fistula may be masked by the absence of significant blood loss at the time of injury[5,26]. Arterial laceration with tamponade of the haemorrhage can result in a false aneurysm[5,27,28]. There may be delayed rupture of the aneurysm but more frequently it presents with symptoms caused by compression of surrounding structures[12,29,30].

Clinical presentation

Classic signs of acute peripheral ischaemia are rare[11,20,31,32]. The commonest acute sign of vascular trauma is a pulse deficit[16,33,34], although the distal pulse may be normal in up to one-quarter of peripheral vascular injuries[11,35]. Other signs which occur with variable frequency include an expanding haematoma, arterial bleeding from the wound, a bruit, or a neurological deficit.

The paucity of unequivocal signs makes a high index of suspicion essential when assessing trauma cases[10,11,36]. Site rather than size of skin laceration should alert the clinician in patients with penetrating injuries overlying vascular structures[28,37]. Specific vessels are noted for their vulnerability: for example, brachial artery occlusion in supracondylar fracture of the humerus, or popliteal artery damage following dislocation of the knee[38–42].

Investigations

Pre-operative investigations have a limited place in the management of obvious vascular trauma[5,11,14,43]. Doppler detection of arterial flow and subsequent pressure measurement is quick and may be useful. Routine pre-operative arteriography can significantly prolong the ischaemic time[20,33,36,44,45] and may have an adverse effect on prognosis[25]. Arteriography is useful in the assessment of patients who are stable with equivocal signs[10,35,46] and may allow conservative management in some[17,27,33,47]. Peroperative arteriography is extremely helpful, particularly in patients with multiple injuries which include fractures proximal or distal to the obvious vascular injury[20,22,41,42,48–50]. Postoperative arteriography is essential in the reassessment of the patient with deteriorating signs[4,10,14,16,33,36,48,51,52].

Treatment

Rapid management of vascular injuries reduces the impact of the two poorest prognostic factors, namely prolonged ischaemia in limb injuries and massive haemorrhage in abdominal injuries[53]. Bleeding can usually be controlled by direct pressure while adequate exposure of the vessel is achieved. Haemostasis must not be obtained by the blind application of forceps[54]. Assessment of the damaged vessel should take place only in an

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operating theatre with facilities to undertake definitive therapy[55]. The patient must be positioned and prepared to allow saphenous vein harvest if necessary[56].

Adequate access and haemostatic control above and below the site of injury are essential before undertaking repair[9]. If exploration has exposed the vascular injury before proximal control has been gained, intraluminal balloon catheters can prevent further haemorrhage[11]. Once haemostasis is achieved the vessel is opened and the extent of any internal disruption is defined; all damaged vessel wall should be excised[33].

Repair can be achieved by direct suture, insertion of a vein patch, or graft interposition[32,33]. The repaired vessel must not be left under tension and its internal diameter must not be narrowed[10]. Stab wounds can usually be dealt with by direct suture or vein patching whereas missile damage or blunt injuries commonly need replacement of a length of vessel with a graft[10,20,45,52].

Tension at the anastomosis cannot be overcome by flexion of joints or rerouting of the native vessel, both of which risk thrombosis during rehabilitation[38]. In an ischaemic limb the collateral circulation may be vital and these vessels should not be divided to increase mobilization. The loss of 1·5 cm of vessel is the maximum length which can be dealt with by mobilization and end-to-end anastomosis[42,56].

Arterial spasm can be entertained as a diagnosis after peroperative radiology has excluded intimal damage. The artery should initially be treated with locally applied papaverine and, if this is unsuccessful, saline distension may be attempted[40,45]. Failure to restore the vessel to its normal calibre is an indication for excision and grafting of the stenosed segment[23].

Major vessels should be ligated only when the procedure is considered to be life saving, or in the presence of gross contamination where subsequent extra-anatomical grafting is possible[32].

Limb amputation can be carried out as a primary or secondary procedure. Primary amputation is performed rarely, but may be indicated in two circumstances: firstly, when soft tissue and bony injury is too extensive to afford useful reconstruction regardless of the vascular viability[10,11,42,48,57]; secondly, when ischaemia has progressed to irreversible tissue necrosis[12]. The 'golden period' of 6 hours[4] during which all limb tissue will revive with adequate perfusion cannot be used as an index for amputation[36]. Other signs of severe ischaemia, such as paralysis and increased muscle turgor, are also unreliable guides, as useful limbs have been salvaged despite these signs[45]. Fixed skin staining is the only undisputed sign of tissue death; amputation before this sign is present may risk loss of a potentially viable limb[12,22].

Secondary amputation is performed either during the early postoperative period when the limb's persistent attachment is thought to threaten the patient's life because of sepsis[8,48,54,58], or later after attempts at rehabilitation have demonstrated that the limb is useless because of ischaemia or major neurological deficit. It is difficult to predict the extent of neurological damage at the time of injury in most cases of combined neurovascular trauma.

Antibiotic prophylaxis and sepsis

Sepsis is the commonest early complication of revascularization[5,8,13,31,33,59]. It is related to insufficient debridement of non-viable and contaminated tissues and inadequate restoration of blood flow[20]. Antibiotics and antitetanus therapy are mandatory[4,56].

Where contamination is gross or when sepsis is present there is an increased risk of anastomotic breakdown. Graft material and anastomoses must be covered by healthy tissue such as peritoneum or omentum in the abdominal cavity or muscle in the limb[4,48,60]. Immediate skin cover is not essential and delayed wound closure should be undertaken whenever contamination has occurred, or when primary closure may increase tissue tension[12,19].

Graft material

Patch repairs of arterial wall can often be performed using a suitable local vein. Longer segments of vein for graft interposition can be harvested from the long saphenous or internal jugular vein[10,13]. Most of the experience of vascular reconstruction has been gained using vein[5,10,54]. There has been reluctance to use synthetic material because of the risks of it becoming infected. Synthetic grafts reduce the reconstruction time[45] and, for defects in intra-abdominal vessels, Dacron (C. R. Bard Inc., Massachusetts, USA) grafts are more appropriate than saphenous vein[9,61,62]. There has been some enthusiasm for the use of polytetrafluoroethylene (PTFE) in potentially contaminated wounds. Vein grafts when infected tend to disrupt throughout their length as well as at the anastomoses[30,62]; PTFE grafts when infected leak only at the anastomoses and haemorrhage may not be torrential owing to prior thrombosis[59,60].

Run off, thrombectomy and anticoagulation

All vessels should be cleared of thrombus using a balloon catheter at the beginning and the end of reconstruction[42,52,54,63]. Patency of distal vessels cannot be safely assessed by simply observing the presence of back bleeding[40]. Copious regional heparin washout should be used after balloon catheterization[11,12,52]. Systemic anticoagulation is contra-indicated when this might cause serious haemorrhage from other injuries[11,56]. If the vascular trauma is localized and completely controlled by the surgical procedure, full anticoagulation should be undertaken with intravenous heparin[8,48,54].

Fasciotomy

Rising tissue tension occludes venous return and eventually impedes arterial filling, both of which are potentially disastrous in a revascularized limb. Decompression fasciotomy is best performed as an open procedure because closed fasciotomy is likely to be incomplete[22,26,36]. The lower limb is more commonly at risk from the compartment syndrome than the upper limb.

Indications for fasciotomy at the time of exploration are delay in revascularization, massive soft tissue damage, increased tissue turgor, coexistent venous damage or venous ligation[10,11,32,64,65]. Some of these indications are present in most cases of vascular trauma and fasciotomy should be carried out in all cases except those with a short ischaemic interval and minimal soft tissue trauma[36]. Fasciotomy may be performed before definitive reconstruction, to allow collateral flow to improve during the reconstruction[26,48]. Postoperative increase in pain in the distal limb, any evidence of decreased perfusion, increasing neurological signs[40], or limb swelling warrant fasciotomy without delay[8,11].

Associated injuries

Associated injuries always take second place to treatment of the vascular injury; observance of this rule will improve success rates after reconstruction[12,16,36,39,42]. In addition, a constant alertness for possible vascular injury will prevent the clinician overlooking acute ischaemia of a limb because of the extent of coexistent soft tissue damage[22]. In cases with both fracture and vessel damage, fixation is best obtained by external devices[20,22,48,51,66,90]. Instability rarely necessitates immediate attention, but if necessary a shunt can be used to bypass the vascular trauma during fixation[35,45,48,52,67].

Postoperative assessment

Once vascular reconstruction is complete and orthopaedic fixation and dressings have been applied, assessment of peripheral perfusion is often difficult. Access to peripheral pulses may be obscured by dressings or soft tissue damage. The Doppler velocimeter, photoplethysmeter[68], or transcutaneous oxygen monitoring[67] can be used to assess skin perfusion. Decreased perfusion should not be treated expectantly; it

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Non-invasive tests can offer haemodynamic information which arteriography does not, and they may eventually replace arteriograms in many situations. At present they have three main roles: helping with the decision to proceed to arteriography; supplementing arteriography with more precise information about blood flow and plaque morphology and following up the results of vascular reconstruction. An additional and more contentious area is the assessment of asymptomatic disease.

We can begin by examining the investigations that might helpfully precede arteriography. In the lower limbs, ankle pressure measurements using the Doppler probe give objective and repeatable data on the severity of ischaemia, and a progressive decrease in ankle systolic pressure may weight the decision to operate[1]. When used with an exercise test the presence of arterial disease can be confirmed or excluded in doubtful cases. Unfortunately, calcification may make the vessels partially or wholly incompressible and spuriously high readings (notably in diabetics) may re-assure the inexperienced. The measurement of toe pressures overcomes this problem since the vessels are rarely calcified, but this investigation is technically more difficult and has its own inaccuracies.

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The other major area in which the non-invasive vascular laboratory plays a part is the assessment of carotid disease, and here the duplex scanner (real time ultrasound plus Doppler) has emerged as an important and powerful tool which is ideally suited to detailed analysis of selected small areas within the blood vessels[5]. It has largely replaced indirect techniques such as periorbital Doppler studies and oculopneumoplethysmography, although these can still be useful for assessing collateral blood supply to the brain when the internal carotid arteries are severely stenosed. The duplex scanner has also superseded the Doppler scanner because it enables detailed assessment of stenoses and plaque morphology as well as flow. Considerable skill is required to use this expensive machine well but, where this is available, some surgeons are now prepared to perform carotid endarterectomy on the evidence provided by duplex scanning alone.

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Vascular trauma

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Civilian vascular trauma is not uncommon. Prompt treatment with modern vascular surgical techniques produces good results.

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Up to 17 per cent of vascular injuries may present late with either an arteriovenous (A–V) fistula or an aneurysm[5,15,18]. The injury which subsequently results in an A–V fistula may be masked by the absence of significant blood loss at the time of injury[5,26]. Arterial laceration with tamponade of the haemorrhage can result in a false aneurysm[5,27,28]. There may be delayed rupture of the aneurysm but more frequently it presents with symptoms caused by compression of surrounding structures[12,29,30].

Clinical presentation

Classic signs of acute peripheral ischaemia are rare[11,20,31,32]. The commonest acute sign of vascular trauma is a pulse deficit[16,33,34], although the distal pulse may be normal in up to one-quarter of peripheral vascular injuries[11,35]. Other signs which occur with variable frequency include an expanding haematoma, arterial bleeding from the wound, a bruit, or a neurological deficit.

The paucity of unequivocal signs makes a high index of suspicion essential when assessing trauma cases[10,11,36]. Site rather than size of skin laceration should alert the clinician in patients with penetrating injuries overlying vascular structures[28,37]. Specific vessels are noted for their vulnerability: for example, brachial artery occlusion in supracondylar fracture of the humerus, or popliteal artery damage following dislocation of the knee[38–42].

Investigations

Pre-operative investigations have a limited place in the management of obvious vascular trauma[5,11,14,43]. Doppler detection of arterial flow and subsequent pressure measurement is quick and may be useful. Routine pre-operative arteriography can significantly prolong the ischaemic time[20,33,36,44,45] and may have an adverse effect on prognosis[25]. Arteriography is useful in the assessment of patients who are stable with equivocal signs[10,35,46] and may allow conservative management in some[17,27,33,47]. Peroperative arteriography is extremely helpful, particularly in patients with multiple injuries which include fractures proximal or distal to the obvious vascular injury[20,22,41,42,48–50]. Postoperative arteriography is essential in the reassessment of the patient with deteriorating signs[4,10,14,16,33,36,48,51,52].

Treatment

Rapid management of vascular injuries reduces the impact of the two poorest prognostic factors, namely prolonged ischaemia in limb injuries and massive haemorrhage in abdominal injuries[53]. Bleeding can usually be controlled by direct pressure while adequate exposure of the vessel is achieved. Haemostasis must not be obtained by the blind application of forceps[54]. Assessment of the damaged vessel should take place only in an

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operating theatre with facilities to undertake definitive therapy[55]. The patient must be positioned and prepared to allow saphenous vein harvest if necessary[56].

Adequate access and haemostatic control above and below the site of injury are essential before undertaking repair[9]. If exploration has exposed the vascular injury before proximal control has been gained, intraluminal balloon catheters can prevent further haemorrhage[11]. Once haemostasis is achieved the vessel is opened and the extent of any internal disruption is defined; all damaged vessel wall should be excised[33].

Repair can be achieved by direct suture, insertion of a vein patch, or graft interposition[32,33]. The repaired vessel must not be left under tension and its internal diameter must not be narrowed[10]. Stab wounds can usually be dealt with by direct suture or vein patching whereas missile damage or blunt injuries commonly need replacement of a length of vessel with a graft[10,20,45,52].

Tension at the anastomosis cannot be overcome by flexion of joints or rerouting of the native vessel, both of which risk thrombosis during rehabilitation[38]. In an ischaemic limb the collateral circulation may be vital and these vessels should not be divided to increase mobilization. The loss of 1·5 cm of vessel is the maximum length which can be dealt with by mobilization and end-to-end anastomosis[42,56].

Arterial spasm can be entertained as a diagnosis after peroperative radiology has excluded intimal damage. The artery should initially be treated with locally applied papaverine and, if this is unsuccessful, saline distension may be attempted[40,45]. Failure to restore the vessel to its normal calibre is an indication for excision and grafting of the stenosed segment[23].

Major vessels should be ligated only when the procedure is considered to be life saving, or in the presence of gross contamination where subsequent extra-anatomical grafting is possible[32].

Limb amputation can be carried out as a primary or secondary procedure. Primary amputation is performed rarely, but may be indicated in two circumstances: firstly, when soft tissue and bony injury is too extensive to afford useful reconstruction regardless of the vascular viability[10,11,42,48,57]; secondly, when ischaemia has progressed to irreversible tissue necrosis[12]. The 'golden period' of 6 hours[4] during which all limb tissue will revive with adequate perfusion cannot be used as an index for amputation[36]. Other signs of severe ischaemia, such as paralysis and increased muscle turgor, are also unreliable guides, as useful limbs have been salvaged despite these signs[45]. Fixed skin staining is the only undisputed sign of tissue death; amputation before this sign is present may risk loss of a potentially viable limb[12,22].

Secondary amputation is performed either during the early postoperative period when the limb's persistent attachment is thought to threaten the patient's life because of sepsis[8,48,54,58], or later after attempts at rehabilitation have demonstrated that the limb is useless because of ischaemia or major neurological deficit. It is difficult to predict the extent of neurological damage at the time of injury in most cases of combined neurovascular trauma.

Antibiotic prophylaxis and sepsis

Sepsis is the commonest early complication of revascularization[5,8,13,31,33,59]. It is related to insufficient debridement of non-viable and contaminated tissues and inadequate restoration of blood flow[20]. Antibiotics and antitetanus therapy are mandatory[4,56].

Where contamination is gross or when sepsis is present there is an increased risk of anastomotic breakdown. Graft material and anastomoses must be covered by healthy tissue such as peritoneum or omentum in the abdominal cavity or muscle in the limb[4,48,60]. Immediate skin cover is not essential and delayed wound closure should be undertaken whenever contamination has occurred, or when primary closure may increase tissue tension[12,19].

Graft material

Patch repairs of arterial wall can often be performed using a suitable local vein. Longer segments of vein for graft interposition can be harvested from the long saphenous or internal jugular vein[10,13]. Most of the experience of vascular reconstruction has been gained using vein[5,10,54]. There has been reluctance to use synthetic material because of the risks of it becoming infected. Synthetic grafts reduce the reconstruction time[45] and, for defects in intra-abdominal vessels, Dacron (C. R. Bard Inc., Massachusetts, USA) grafts are more appropriate than saphenous vein[9,61,62]. There has been some enthusiasm for the use of polytetrafluoroethylene (PTFE) in potentially contaminated wounds. Vein grafts when infected tend to disrupt throughout their length as well as at the anastomoses[30,62]; PTFE grafts when infected leak only at the anastomoses and haemorrhage may not be torrential owing to prior thrombosis[59,60].

Run off, thrombectomy and anticoagulation

All vessels should be cleared of thrombus using a balloon catheter at the beginning and the end of reconstruction[42,52,54,63]. Patency of distal vessels cannot be safely assessed by simply observing the presence of back bleeding[40]. Copious regional heparin washout should be used after balloon catheterization[11,12,52]. Systemic anticoagulation is contra-indicated when this might cause serious haemorrhage from other injuries[11,56]. If the vascular trauma is localized and completely controlled by the surgical procedure, full anticoagulation should be undertaken with intravenous heparin[8,48,54].

Fasciotomy

Rising tissue tension occludes venous return and eventually impedes arterial filling, both of which are potentially disastrous in a revascularized limb. Decompression fasciotomy is best performed as an open procedure because closed fasciotomy is likely to be incomplete[22,26,36]. The lower limb is more commonly at risk from the compartment syndrome than the upper limb.

Indications for fasciotomy at the time of exploration are delay in revascularization, massive soft tissue damage, increased tissue turgor, coexistent venous damage or venous ligation[10,11,32,64,65]. Some of these indications are present in most cases of vascular trauma and fasciotomy should be carried out in all cases except those with a short ischaemic interval and minimal soft tissue trauma[36]. Fasciotomy may be performed before definitive reconstruction, to allow collateral flow to improve during the reconstruction[26,48]. Postoperative increase in pain in the distal limb, any evidence of decreased perfusion, increasing neurological signs[40], or limb swelling warrant fasciotomy without delay[8,11].

Associated injuries

Associated injuries always take second place to treatment of the vascular injury; observance of this rule will improve success rates after reconstruction[12,16,36,39,42]. In addition, a constant alertness for possible vascular injury will prevent the clinician overlooking acute ischaemia of a limb because of the extent of coexistent soft tissue damage[22]. In cases with both fracture and vessel damage, fixation is best obtained by external devices[20,22,48,51,66,90]. Instability rarely necessitates immediate attention, but if necessary a shunt can be used to bypass the vascular trauma during fixation[35,45,48,52,67].

Postoperative assessment

Once vascular reconstruction is complete and orthopaedic fixation and dressings have been applied, assessment of peripheral perfusion is often difficult. Access to peripheral pulses may be obscured by dressings or soft tissue damage. The Doppler velocimeter, photoplethysmeter[68], or transcutaneous oxygen monitoring[67] can be used to assess skin perfusion. Decreased perfusion should not be treated expectantly; it should be assessed by arteriography[48]. If arteriography is impractical the reconstruction should be re-explored urgently.

Venous injuries and reconstruction

The observed incidence of venous injury is lower than that for arteries, because the signs are few and may go unnoticed[69]. Until recently, ligation was the universal treatment for venous damage. Complications of ligation, related to venous hypertension, have been noted in the lower limb, but very rarely in the upper limb[7,37,70]. Recently, attempts have been made to reconstruct major veins in the lower limb[71]. Lacerations can be treated with direct suture and this should be attempted wherever possible. Grafting is required if there has been a significant loss of vein wall[7,72,73]. Various techniques have been described to convert a saphenous vein into a tube of greater diameter[11,19,64,74]. Major caval defects can be repaired using a 'panel' graft of opened segments of long saphenous vein sutured together or a Dacron® tube graft can be inserted[75]. Patency rates are improved if systemic anticoagulation is instituted at the time of repair[64]. No increase in venous embolic complications has been recorded following venous repair[42,44]. Although these techniques are correct in principle, reconstruction may be impracticable if anaesthesia has to be prolonged unduly, excessive haemorrhage is encountered while attempting repair and if there is pressing need to attend to associated injuries[64,76].

Specific injuries

Neck vessels

Trauma to the neck vessels accounts for 5–10 per cent of major vascular injuries[11,12,77]. The overall mortality ranges from 11 to 21 per cent[76,78,79]; central neurological signs are the most significant index of a poor prognosis[63,76,78]. The majority of cases are due to penetrating trauma. Blunt injuries most commonly occur in RTAs with hyperextension and rotation of the neck which stretches the vascular sheath as it passes over the cervical vertebrae[19,77,80]. The common and internal carotid arteries are the vessels most often traumatized; injury to the external carotid, vertebral and innominate arteries occurs less frequently[11,78]. Injury to the great veins of the neck occurs in association with arterial trauma in approximately one-third of cases[43,46,78].

Presentation and investigations. The rule that every neck injury which penetrates the platysma should be explored[43,55] has been modified in the light of reports that the negative exploration rate can be safely reduced by as much as 50 per cent by careful clinical assessment and arteriography[37,46,57,76]. Specific criteria for neck exploration are an obstructed airway or central neurological signs[27,37,76].

Most casualties with neck vessel injuries are haemodynamically stable and the site of injury can be safely defined by preoperative arteriography[28,55,79]. A false aneurysm or A–V fistula may present at a late stage with cerebral embolic episodes[28,77].

Treatment. The neck is commonly divided into zones: Zone I below the clavicle, Zone III above the mandible and Zone II in between[27,37]. Most trauma occurs to the common carotid artery in Zone II and is easily accessible by incising along the anterior border of the sternomastoid muscle. Planning the approach to Zones I and III is aided by arteriography[28,63,78]. In Zone III subluxation of the mandible may be required for access to the distal internal carotid artery[78] and in Zone I partial median sternotomy is often essential to gain proximal control of the great vessels[37]. Access to the vertebral artery requires medial displacement of the carotid sheath so that the artery can be exposed as it ascends in the vertebral foramina[76].

In the majority of cases there are no associated neurological signs[11,78] and vascular repair can be achieved by direct suture[79]. When there is a defect in the carotid artery wall a vein graft, or external carotid artery interposition, can be used[78]. A vein graft can be taken from the ipsilateral internal jugular vein.

Numerous reports have demonstrated that central neurological signs are not a contra-indication to revascularization[32,43,44,55,57,76,80,81]. Although there is a potential risk of haemorrhage into an ischaemic area of cortex[74], revascularization tends to improve the neurological status in patients who are precomatose, whereas comatose patients tend to do badly regardless of surgical intervention[28,63,78].

Shunts are recommended during repair of internal carotid artery injuries[37] but are not needed for common carotid artery injury[63]. The vessels distal to the trauma should be cleared of clot using a balloon catheter before revascularization[63].

Ligation of the common and internal carotid arteries is accompanied by a mortality rate of approximately 50 per cent[11,79]. The poor prognosis in this group is due to the inclusion of patients in coma and individuals in a poor haemodynamic state where ligation has been undertaken to achieve rapid haemostasis[43]. The vertebral and external carotid arteries can safely be ligated, but formal exposure of the injury vessel is needed since haemorrhage is equally profuse from the distal and proximal ends.

Venous injury is repaired if possible by lateral suture, but ligation is usually uneventful[12,69,76].

Upper limb

Between one-third and one-half of all vascular injuries occur in the upper limbs[5,10,12,44,54]. The brachial artery is the most commonly injured vessel followed in order of frequency by the forearm, axillary and subclavian vessels[8,28,54]. Penetrating injuries are more common than blunt injuries; the latter are usually accompanied by skeletal or nerve injury[82–85].

The incidence of amputation was about 40 per cent when all vascular injuries were ligated[1,41]. Since revascularization has been performed routinely, only 3–4 per cent of patients require amputation[8,41]. The most important prognostic indicator in upper limb injury is not viability but function, the loss of function being due to claudication or associated nerve injuries[16,54,57,86,87].

It is rarely possible at the time of presentation to predict which limbs will eventually be useless and require secondary amputation[34,54]. Even in a flail limb, primary amputation is rarely recommended because revascularization may ensure that there is a useful stump upon which to attach a prosthesis[87].

Presentation and investigations. Clinical signs of vascular trauma in the upper limb are very variable with pulse deficit being the commonest sign[54]. Subclavian and axillary injuries often produce few local signs because a haematoma or arterial bleeding are masked by the surrounding tissues[41] and because of the substantial collateral circulation there may be no pulse deficit[16,26,28,30,84,88]. Proximal vessel injury should be considered in upper limb trauma with an associated brachial plexus injury[41,89,90] and in posteriorly displaced first rib fractures[16,89,91,92]. Symptoms of ischaemia secondary to vascular damage in the forearm depend on the patency of the palmar arch, assessed by the Allen test[88] and the extent to which soft tissue damage reduces collateral circulation[31]. Isolated damage to either the radial or the ulnar artery with an intact palmar arch rarely produces ischaemia. Damage to both vessels usually leaves the forearm poorly perfused and liable to claudication. Missed subclavian or axillary artery injury may present as a false aneurysm or fistula[5]. The first sign may be a progressive peripheral nerve palsy as the expanding aneurysm stretches the brachial plexus[30,93].

The collateral circulation usually maintains limb viability, allowing arteriography to be performed pre-operatively in most cases[26,90].

Treatment. Control of the innominate and right subclavian vessels is gained by a supraclavicular and partial median sternotomy incision[26,28,38]. This can be extended by dividing the sternum transversely at the level of the third intercostal space to create a trap-door exposure[12]. The proximal subclavian artery on the left is approached by an anterolateral third intercostal space thoracotomy[90]. Distal control of the axillary artery can be gained from an infraclavicular incision dividing the insertion of the pectoral muscles as necessary[41]. Collateral circulation makes control of arm vessels more difficult, and dissection directly on to the injury is appropriate[54].

Graft material can often be harvested from available arm veins[38],[94]. Alternatively PTFE grafts have been used successfully in the axilla[41]. Forearm vessels should be repaired using microvascular techniques when more than one vessel is involved or when associated soft tissue damage may have diminished the available collateral supply[31].

Restoring venous continuity is desirable[26,41] but not essential. Following proximal venous ligation, even of the subclavian vein, oedema is usually transient[8,12,59,69]. Fasciotomy should be considered where forearm vessels have been repaired[31], although postoperative elevation of the arm allows most transient oedema to resolve[5,32].

Abdomen

Trauma to the abdominal vessels is uncommon[71,95]. When injury does occur the haemorrhage is often so torrential that the diagnosis is made post mortem[72,73,96,97]. Improvements in patient retrieval and resuscitation now enable many patients who would previously have been roadside fatalities to reach hospital[9,14,98].

The inferior vena cava (IVC) and aorta are fixed in position by their lumbar branches and are therefore more susceptible to injury than the rest of the intraperitoneal circulation[32,44]. If the posterior peritoneum remains intact, haematoma formation may tamponade further bleeding[18]. Injury to mesenteric vessels can cause massive haemorrhage as there is no means of achieving tamponade[74,95,99,100]. The iliac vessels are protected by the pelvis but can be damaged by displaced pelvic fractures, with the veins being injured more commonly than the arteries.

Mortality from abdominal vascular trauma remains high at between 30 and 73 per cent[75,97–99,101]. The presence of other visceral injuries and subsequent sepsis is associated with a particularly poor prognosis[7,9,61,72,73,75,95,98,102].

Presentation and investigations. The diagnosis of vascular trauma is usually obvious because of the systemic signs of blood loss and peritoneal irritation. Tamponade of the haemorrhage by the peritoneum may mask signs although an abdominal bruit may be heard[18,101]. If the diagnosis is missed at this stage there may be late presentation with a false aortic aneurysm[18,29].

Blunt injury can cause intimal disruption in the aorta and presentation with acute peripheral ischaemia without signs of haemorrhage[18]. Rarely, such trauma may cause acute vena caval thrombosis[103].

Iliac vessel trauma often produces no specific signs of vascular injury. Pulse deficits or bruits are present in less than 25 per cent of cases. Commonly there is a subumbilical entry wound associated with peritonism and hypovolaemia[7].

Peritoneal lavage can improve diagnostic accuracy[104,105] but is misleading in those with haemorrhage confined to the retroperitoneal space.

Treatment. Patients with signs of hypotension or peritoneal irritation and those with penetrating gun or missile injuries should be explored. Individuals with blunt injuries or knife wounds where the signs are equivocal can be treated expectantly[9].

Rapid vascular control may be difficult to achieve. The aorta can be clamped within the abdomen, but in moribund patients unresponsive to initial fluid resuscitation, the lower thoracic aorta can be clamped temporarily through a left arterolateral thoracotomy[7,9,97,102,104].

IVC injuries can be controlled by direct pressure, but particular difficulty is experienced in the control of the retrohepatic IVC. Liver mobilization, including extension of the exploration into the chest by dividing the diaphragm, allows adequate access[73,74,106], but the haemorrhage often becomes torrential as the liver tamponade is released. Such retrohepatic injury can be isolated using the Pringle manoeuvre combined with insertion of an intraluminal venous shunt from the infrahepatic IVC to the right atrium[74,107].

Any extensive retroperitoneal haematoma should be explored, apart from non-pulsatile non-expanding haematomas arising out of the pelvis [32,61,74,75,101]. Repair of the abdominal aorta can commonly be achieved by direct suture; where tissue loss requires grafting, Dacron should be used. Defects in visceral arteries should be replaced with saphenous vein[100]. Superior mesenteric artery reconstruction is mandatory, but the inferior mesenteric artery and the coeliac axis can usually be ligated without consequence[57,97].

IVC injuries should always be repaired where possible[75]. Although this may decrease the diameter it will increase flow rate. Posterior wall tears can be repaired from within the lumen through an anterior venotomy[72,75]. Ligation of the infrarenal IVC is occasionally required for haemostasis and is usually not complicated by chronic oedema[73,104]. Suprarenal ligation of the inferior vena cava is usually fatal[73]. Portal and superior mesenteric vein injuries should be repaired whereas other mesenteric veins can be ligated[74,75]. Ligation of pelvic veins only rarely causes persistent postoperative lower limb oedema[7].

Contamination from associated gut injuries may endanger vascular repair within the peritoneal cavity. Thus, in the case of an aortic injury, an axillo-bifemoral bypass graft may be the safest means of revascularizing the lower limbs[32].

Renal arterial injuries are usually secondary to blunt trauma. If damage to the kidneys is suspected an intravenous urogram should be obtained. Confirmation that non-function of one kidney is due to renal artery thrombosis requires mid-stream aortography[108]. The left renal pedicle is more commonly injured. Unfortunately, the kidney is frequently infarcted and therefore revascularization is only successful in one-third of cases[108]. In the presence of a normal second kidney, exploration of a contralateral renal artery thrombosis should be considered only in patients whose condition is completely stable. Late nephrectomy may have to be considered in subjects with an atrophied kidney who develop significant hypertension[108,109].

Vascular injury in the pelvis can cause persistent blood loss, the source of which is either unidentifiable or inaccessible[110]. The haemorrhage can be controlled with meticulous packing. Packs should be left *in situ* for 24 hours and then removed under general anaesthetic to allow reassessment and repacking if necessary. Recently, rapid control of bleeding has been reported following embolization of the internal iliac artery and its branches[32,110–112].

Lower limb

Lower limb injuries account for the majority of cases of vascular trauma in accident admissions, battle casualties and victims of terrorist bombing[11,12]. In the Second World War, when arterial reconstruction was seldom attempted, ligation of the femoral artery and the popliteal artery incurred distal amputation rates of 55 and 73 per cent respectively[1]. Since reconstruction has become universal practice, amputation rates have decreased dramatically. The amputation rate following popliteal artery injuries in Korean and Vietnam war casualties was 30 per cent[2,3]. In recent reports of popliteal reconstruction or bypass in civilian practice, amputation rates of between 0 and 44 per cent have been recorded[39,42,48,113,114]. The need for amputation depends upon a variety of factors, the most important being delay from injury to revascularization[25,42,45,51].

Presentation and investigations. The diagnosis is more obvious than in the upper limb as a pulse deficit is present in 60 per cent of cases[16,32,33,48,113]. Specific injuries which should arouse a high index of suspicion are penetrating injuries to the femoral triangle[60] or the popliteal fossa, and blunt injuries causing fracture or dislocation around the knee[39,48,115]. Up to 40 per cent of serious knee injuries have associated popliteal artery damage and arteriography should be considered in every case[42,57,66,116,117].

Treatment. Control of the common femoral artery may require division of the inguinal ligament or extraperitoneal exposure of the external iliac artery in the iliac fossa. The popliteal vessels can be approached from the medial[22] or the posterior aspect[19,56]. The posterior approach allows wide access but necessitates the patient being prone which may not be possible in the presence of associated injuries[11].

A vein patch rather than lateral suture is necessary for most lower limb arterial repairs to avoid narrowing[56]. The vein should be harvested from the contralateral limb as the ipsilateral long saphenous vein may be the major route of venous drainage in a severely injured limb[19]. An isolated tibial arterial injury may be treated by ligation but loss of both the anterior and posterior tibial arteries incurs an amputation rate of up to 69 per cent[1]. Repair by vein patch or graft interposition reduces the risk of amputation or subsequent morbidity from claudication[25,118].

Venous damage is less commonly reported than arterial injury and usually accompanies more severe trauma[48,52,61]. Venous repair was shown to reduce leg oedema significantly in Vietnam[61,71]. Ligation of popliteal veins occasionally produces permanent oedema[11,70]. Femoral vein ligation causes immediate postoperative lower limb oedema but this normally resolves[63]. Saphenous vein graft has also been used where there is loss of vein wall, but systemic heparinization is essential for continued patency, and this may be problematic in patients with extensive trauma[64].

Fasciotomy is required in between one-third and one-half of lower limb vascular injuries[12,33], in particular those injuries involving the popliteal vessels[19,64]. Missed compartment syndromes are often catastrophic[8,20,25,34] and routine fasciotomy has therefore been adopted by many centres[21,42,51,113]. Calf fasciotomy must be performed through a full-length skin incision over the lateral aspect of the fibula and by retraction of the skin incision all four calf compartments can then be decompressed[32,119].

Conclusions

An early diagnosis of vascular injury is essential for the success of subsequent repair. The clinician must be constantly alert to the possibility of vessel damage, particularly in patients with multisystem trauma.

Once detected, repair of the damaged artery takes precedence over any musculoskeletal injuries. Further assessment of the vascular injury should be carried out in surroundings that permit full control and definitive repair of the injury. For limb injuries, angiography should be performed during surgery to reduce the overall ischaemic time.

Patient survival and limb function have steadily improved as expertise in vascular reconstruction has become available at district general hospital level. Arterial ligation should be carried out only where prompt haemostasis is essential as a life-saving measure. The emphasis on vascular reconstruction may encourage prolonged efforts to repair vascular damage in an unsalvageable limb where subsequent sepsis may then prejudice patient survival. Therefore, in cases with severe soft tissue destruction and combined neurological and vascular damage, primary amputation may be the best option.

Successful reconstruction of an isolated arterial injury should always be possible as long as basic vascular surgical techniques are applied. This should result in complete restoration of function with minimal long-term morbidity. The clear message from all large series is that reducing the delay between injury and reconstruction is the most important factor in improving prognosis.

References

1. DeBakey ME, Simeone FA. Battle injuries of arteries in World War II: an analysis of 2471 cases. *Ann Surg* 1946; **123**: 534–79.
2. Hughes CW, Bowers WF. *Traumatic Lesions of Peripheral Vessels*. Springfield, Illinois: Charles C Thomas, 1961.
3. Rich NM, Spencer FC. *Vascular Trauma*. Philadelphia: WB Saunders Company, 1978.
4. Adinolfi MF, Hardin WD, O'Connell RC, Kerstein MD. Amputations after vascular trauma in civilians. *South Med J* 1983; **76**: 1241–3.
5. Adar R, Schramek A, Khodadadi J, Zweig A, Gokman L, Romanoff H. Arterial combat injuries of the upper extremity. *J Trauma* 1980; **20**: 297–301.
6. Barros D'Sa AAB. A decade of missile-induced vascular trauma. *Ann R Coll Surg Engl* 1982; **64**: 37–44.
7. Ryan W, Snyder W, Bell T, Hunt J. Penetrating injuries of the iliac vessels. *Am J Surg* 1982; **144**: 642–5.
8. Hardin WD, O'Connell RC, Adinolfi MF, Kerstein MD. Traumatic arterial injuries of the upper extremity: determinants of disability. *Am J Surg* 1985; **150**: 266–70.
9. Millikan JS, Moore EE. Critical factors in determining mortality from abdominal aortic trauma. *Surg Gynecol Obstet* 1985; **160**: 313–16.
10. Thomas WEG, Baird RN. Arterial injuries in two Bristol hospitals from 1974 to 1980. *Injury* 1983; **15**: 30–4.
11. Bergentz SE, Bergqvist D, Ericsson BF. Vascular trauma. *Acta Chir Scand* 1983; **149**: 1–10.
12. Robbs JV, Baker LW. Major arterial trauma: review of experience with 267 injuries. *Br J Surg* 1978; **65**: 532–8.
13. Feliciano DV, Bitondo CG, Mattox KL *et al.* Civilian trauma in the 1980's. *Ann Surg* 1984; **199**: 717–23.
14. Sharma PVP, Babu SC, Shah PM, Clauss RH. Changing patterns in civilian artery injuries. *J Cardiovasc Surg* 1985; **26**: 7–11.
15. Drapanas T, Hewitt RL, Weichert RF, Smith AD. Civilian vascular injuries: a critical appraisal of three decades of management. *Ann Surg* 1970; **172**: 351–60.
16. Sturm JT, Bodily KC, Rothenberger DA, Perry JF. Arterial injuries of the extremities following blunt trauma. *J Trauma* 1980; **20**: 933–6.
17. Perry MO, Snyder WH, Thal ER. Carotid artery injuries caused by blunt trauma. *Ann Surg* 1980; **192**: 74–7.
18. Lassonde J, Laurendeau F. Blunt injury of the abdominal aorta. *Ann Surg* 1981; **194**: 745–8.
19. O'Reilly MJG, Hood JM, Livingston RH, Irwin JWS. Penetrating injuries of the popliteal artery. *Br J Surg* 1978; **65**: 789–92.
20. Ransom KJ, Shantey CH, Soderstrom CA, Cowley RA. Management of arterial injuries in blunt trauma of the extremity. *Surg Gynecol Obstet* 1981; **153**: 241–6.
21. Slaney G, Ashton F. Arterial injuries and their management. *Postgrad Med J* 1971; **47**: 257–69.
22. Meek AC, Robbs JV. Vascular injury associated with bone and joint trauma. *Br J Surg* 1984; **71**: 341–4.
23. Samson R, Pasternak BM. Traumatic arterial spasm—rarity or nonentity. *J Trauma* 1980; **20**: 607–9.
24. Friedman RJ, Jupiter JB. Vascular injuries and closed extremity fractures in children. *Clin Orthop* 1984; **188**: 112–19.
25. Porter MF. Arterial injuries in an accident unit. *Br J Surg* 1967; **54**: 100–5.
26. Lim LT, Saletta JD, Flanigan DP. Subclavian and innominate artery trauma. *Surgery* 1979; **86**: 890–6.
27. Dunbar LL, Adkins RB, Waterhouse G. Penetrating injuries to the neck, selective management. *Am Surg* 1984; **50**: 198–204.
28. Busuttil RW, Acker B. Management of injuries to the brachiocephalic vessels. *Surg Gynecol Obstet* 1982; **154**: 737–43.
29. Bass A, Papa M, Morag B, Adar R. Aortic false aneurysms following blunt trauma of the abdomen. *J Trauma* 1983; **23**: 1072–3.
30. Robbs JV, Naidoo KS. Nerve compression injuries due to traumatic false aneurysm. *Ann Surg* 1984; **200**: 80–2.
31. Lee RE, Obeid FN, Horst HM, Bivins BA. Acute penetrating

arterial injuries of the forearm, ligation or repair? *Am Surg* 1985; **51**: 318–24.

32. Robbs JV, Baker LW. Cardiovascular trauma. *Curr Probl Surg* 1984; **XXI**: 20–87.
33. Snyder WH, Watkins WL, Whiddon LL, Bone GE. Civilian popliteal artery trauma: an eleven year experience with 83 injuries. *Surgery* 1979; **85**: 101–7.
34. Peacock JB, Proctor HJ. Factors limiting extremity function following vascular injury. *J Trauma* 1977; **17**: 532–5.
35. Gelberman RH, Menon J, Fronek A. The peripheral pulse following arterial injury. *J Trauma* 1980; **20**: 948–50.
36. Allen MJ, Nash RJ, Ioannidies TT, Bell PRF. Major vascular injuries associated with orthopaedic injuries to the lower limb. *Ann R Coll Surg Engl* 1984; **66**: 101–4.
37. Lundy LJ, Mandal AK, Lou MA, Alexander JL. Experience in selective operations in the management of penetrating wounds of the neck. *Surg Gynecol Obstet* 1978; **147**: 845–8.
38. Richardson JD, Smith JM, Grover FL, Arom KV, Trinkle JK. Management of subclavian and innominate artery injuries. *Am J Surg* 1977; **134**: 780–4.
39. McCabe CJ, Ferguson CM, Ottinger LW. Improved limb salvage in popliteal artery injuries. *J Trauma* 1983; **23**: 982–5.
40. Morton HJ, Southgate WA, DeWeese JA. Arterial injuries of the extremities. *Surg Gynecol Obstet* 1966; **120**: 611–27.
41. Graham JM, Mattox KL, Feliciano DV, DeBakey ME. Vascular injuries of the axilla. *Ann Surg* 1982; **195**: 232–8.
42. Fabian TC, Turkleson ML, Connelly TL, Stone HH. Injury to the popliteal artery. *Am J Surg* 1982; **143**: 225–8.
43. Padberg FT, Hobson RW, Yeager RA, Lynch TG. Penetrating carotid arterial trauma. *Am Surg* 1984; **50**: 277–82.
44. Kjellstrom T, Risberg B. Vascular trauma. *Acta Chir Scand* 1980; **146**: 261–5.
45. Shah DM, Naraynsingh V, Leather RP, Corson JD, Karmody AM. Advances in the management of acute popliteal vascular blunt injuries. *J Trauma* 1985; **25**: 793–7.
46. Hiatt JR, Busuttil RW, Wilson SE. Impact of routine arteriography on management of penetrating neck injuries. *J Vasc Surg* 1984; **1**: 860–6.
47. Smith PL, Lim WN, Ferris EJ, Casali RE. Emergency arteriography in extremity trauma: assessment of indications. *Am J Radiol* 1981; **137**: 803–7.
48. Snyder WH. Vascular injuries near the knee: an updated series and overview of the problem. *Surgery* 1982; **91**: 502–6.
49. Graham JM, Feliciano DV, Mattox KL. Combined brachial, axillary, and subclavian artery injuries of the same extremity. *J Trauma* 1980; **20**: 899–910.
50. Roberts RM, String ST. Arterial injuries in extremity shotgun wounds: requisite factors for successful management. *Surgery* 1984; **96**: 902–8.
51. Alberty RE, Goodfried G, Boyden AM. Popliteal artery injury with fractural dislocation of the knee. *Am J Surg* 1981; **142**: 36–40.
52. Orcutt MB, Levine BA, Root HD, Sirinek KR. The continuing challenge of popliteal vascular injuries. *Am J Surg* 1983; **146**: 758–61.
53. Ekbom GA, Towne JB, Majewksi JT, Woods JH. Intra-abdominal vascular trauma—a need for prompt operation. *J Trauma* 1981; **21**: 1040–4.
54. Borman KR, Snyder WH, Weigelt JA. Civilian arterial trauma of the upper extremity. *Am J Surg* 1984; **148**: 796–9.
55. Sankaran S, Walt AJ. Penetrating wounds of the neck: principles and some controversies. *Surg Clin North Am* 1977; **57**: 139–50.
56. Abernathy C, Dickinson TC, Lokey H. Management of popliteal artery injuries. *Surg Clin North Am* 1979; **59**: 507–15.
57. Saide R, Jacobsen DC, Block JH, Phillips CN. Management of peripheral vascular trauma. *Am Surg* 1981; **47**: 429–38.
58. Shah PM, Ito K, Clauss RH, Babu SC, Reynolds BM, Stahl WM. Expanded microporous polytetrafluoroethylene (PTFE) grafts in contaminated wounds: experimental and clinical study. *J Trauma* 1983; **23**: 1030–3.
59. Mattox KL, Rea J, Ennix CL, Beall AC, DeBakey ME. Penetrating injuries to the iliac arteries. *Am J Surg* 1978; **136**: 663–7.
60. Kurzweg FT. Vascular injuries associated with penetrating wounds of the groin. *J Trauma* 1980; **20**: 214–19.
61. Myles RA, Yellin AE. Traumatic injuries of the abdominal aorta. *Am J Surg* 1979; **138**: 273–7.
62. Shah DM, Leather RP, Corson JD, Karmody AM. Polytetrafluoroethylene grafts in the rapid reconstruction of acute contaminated peripheral vascular injuries. *Am J Surg* 1984; **148**: 229–33.
63. Ledgerwood AM, Mullins RJ, Lucas CE. Primary repair vs ligation for carotid artery injuries. *Arch Surg* 1980; **115**: 488–93.
64. O'Reilly MJG, Hood JM, Livingston RH, Irwin JWS. Penetrating injuries of the popliteal vein: a report on 34 cases. *Br J Surg* 1980; **67**: 337–40.
65. Ross SE, Ransom KJ, Shatney CH. The management of venous injuries in blunt extremity trauma. *J Trauma* 1985; **25**: 150–3.
66. Mendonca JM, Norton de Matos A. Arterial injuries associated with trauma to the knee. *Am J Surg* 1984; **147**: 210–11.
67. Cram HB, Shoemaker WC. Diagnosis of major peripheral arterial trauma by transcutaneous oxygen monitoring. *Am J Surg* 1984; **147**: 776–80.
68. Lamb SL, Anderson J, Seifert KB, Blackshear WM. The optimum method of toe measurement. *Bruit* 1983; **VII**: 26–32.
69. Graham JM, Feliciano DV, Mattox KL, Beall AC. Innominate vascular injury. *J Trauma* 1982; **22**: 647–55.
70. Hardin WD Jr, Adinolfi MF, O'Connell RC, Kerstein MD. Management of traumatic peripheral vein injuries. Primary repair or vein ligation. *Am J Surg* 1982; **144**: 235–8.
71. Rich NM. Principles and indications for primary venous repair. *Surgery* 1982; **91**: 492–6.
72. Kudsk KA, Bongard F, Lim RC. Determinants of survival after vena caval injury. *Arch Surg* 1984; **119**: 1009–12.
73. Turpin I, State D, Schwartz A. Injuries to the inferior vena cava and their management. *Am J Surg* 1977; **134**: 25–32.
74. Cohen D, Johansen K, Cottingham K, Clayson K, Simonowitz D. Trauma to major visceral veins: an underemphasised cause of accident mortality. *J Trauma* 1980; **20**: 928–32.
75. Mattox KL. Abdominal venous injuries. *Surgery* 1982; **91**: 497–501.
76. Demetriades D, Stewart M. Penetrating injuries of the neck. *Ann R Coll Surg Engl* 1985; **67**: 71–4.
77. Davis JM, Zimmerman RA. Injury of the carotid and vertebral arteries. *Neuroradiology* 1983; **25**: 55–69.
78. Brown MF, Graham JM, Feliciano DV, Mattox KL, Beall AC, DeBakey ME. Carotid artery injuries. *Am J Surg* 1982; **144**: 748–52.
79. Karlin RM, Marks C. Extracranial carotid artery injury. Current surgical management. *Am J Surg* 1983; **146**: 225–7.
80. Dragon R, Saranchak H, Lakin P, Strauch G. Blunt injuries to the carotid and vertebral arteries. *Am J Surg* 1981; **141**: 497–500.
81. Robbs JV, Human RR, Rajaruthnam P, Duncan H, Vawda I, Baker LW. Neurological deficit and injuries involving the neck arteries. *Br J Surg* 1983; **70**: 220–2.
82 Hayes JM, Van Winkle GN. Axillary artery injury with minimally displaced fracture of the neck of the humerus. *J Trauma* 1983; **23**: 431–3.
83 Baratta JB, Lim V, Mastromonaco E, Edillon EL. Axillary artery disruption secondary to anterior dislocation of the shoulder. *J Trauma* 1983; **23**: 1009–11.
84. Drury JK, Scullion JE. Vascular complications of anterior dislocation of the shoulder. *Br J Surg* 1980; **67**: 579–81.
85. Zuckerman JD, Flugstad DL, Teitz CC, King HA. Axillary artery injury as a complication of proximal humeral fractures. *Clin Orthop* 1984; **189**: 234–7.
86. Visser PA, Hermreck AS, Pierce GE, Thomas JH, Hardin CA. Prognosis of nerve injuries incurred during acute trauma to peripheral arteries. *Am J Surg* 1980; **140**: 596–9.
87. Tomaszek DE. Combined subclavian artery and brachial plexus injuries from blunt upper-extremity trauma. *J Trauma* 1984; **24**: 161–3.
88. Gelberman RH, Nunley JA, Koman LA *et al.* The results of radial and ulnar arterial repair in the forearm. Experience in three medical centers. *J Bone Joint Surg* 1982; **64**: 383–7.
89. Phillips EH, Rogers WF, Gaspar MR. First rib fractures: incidence of vascular injury and indications for angiography. *Surgery* 1981; **89**: 42–7.
90. Zelenock GB, Kazmers A, Graham LM *et al.* Non penetrating subclavian artery injuries. *Arch Surg* 1985; **120**: 685–92.
91. Livoni JP, Barcia TC. Fracture of the first and second rib: incidence of vascular injury relative to type of fracture. *Radiology* 1982; **145**: 31–3.
92. Fisher RG, Ward RE, Ben-Menachem Y, Mattox KL, Flynn TC. Arteriography and the fractured first rib: too much for too little? *Am J Radiol* 1982; **138**: 1059–62.
93. Gallen J, Wiss DA, Cantelmo N, Menzoin JO. Traumatic pseudoaneurysm of the axillary artery: report of three cases and

literature review. *J Trauma* 1984; **24**: 350–4.

94. Reichle FA, Golsorkhi M. Diagnosis and management of penetrating arterial and venous injuries in the extremities. *Am J Surg* 1980; **40**: 365–7.
95. Graham JM, Mattox KL, Beall AC, DeBakey ME. Injuries to the visceral arteries. *Surgery* 1978; **84**: 835–9.
96. Bergqvist D, Takolander R. Aortic occlusion following blunt trauma of the abdomen. *J Trauma* 1981; **21**: 319–22.
97. Graham JM, Mattox KL, Beall AC, DeBakey ME. Traumatic injuries of the inferior vena cava. *Arch Surg* 1978; **113**: 413–17.
98. Halpern NB, Aldrete JS. Factors influencing mortality and morbidity from injuries to the abdominal aorta and inferior vena cava. *Am J Surg* 1979; **137**: 384–8.
99. Courcy PA, Brotman S, Oster-Granite ML, Soderstrom CA, Siegel JH, Cowley RA. Superior mesenteric artery and vein injuries from blunt abdominal trauma. *J Trauma* 1984; **24**: 843–5.
100. Lucas AE, Richardson JD, Flint LM, Polk HC Jr. Traumatic injury of the proximal superior mesenteric artery. *Ann Surg* 1981; **193**: 30–4.
101. Mattox KL, Whisennand HH, Espada R, Beall AC. Management of acute combined injuries to the aorta and inferior vena cava. *Am J Surg* 1975; **130**: 720–4.
102. Millikan JS, Moore EE. Outcome of resuscitative thoracotomy and descending aortic occlusion performed in the operating room. *J Trauma* 1984; **24**: 387–92.
103. Campbell DN, Liechty RD, Rutherford RB. Traumatic thrombosis of the inferior vena cava. *J Trauma* 1981; **21**: 413–5.
104. Millikan JS, Moore EE, Cogbill TH, Kashuk JL. Inferior vena caval injuries—a continuing challenge. *J. Trauma* 1983; **23**: 207–12.
105. Borman KR, Aurbakken CM, Weigelt JA. Treatment priorities in combined blunt abdominal and aortic trauma. *Am J Surg* 1982; **144**: 728–31.
106. Madding GF, Lim RC, Kennedy PA. Hepatic and vena caval injuries. *Surg Clin North Am* 1977; **57**: 275–89.
107. Peterson NE, Millikan JS, Moore EE. Combined renal and vena caval trauma: a review of personal and recorded experience. *J Urol* 1985; **133**: 567–74.
108. Clark DE, Georgitis JW, Ray FS. Renal artery injuries caused by blunt trauma. *Surgery* 1981; **90**: 87–96.
109. Ernst D, Windsor CW. Traumatic renal artery occlusion producing hypertension. *Br J Surg* 1981; **68**: 19–20.
110. Owen DR, Hodgson PE. Control of haemorrhage following missile wound to the pelvis. *J Trauma* 1980; **20**: 906–8.
111. Ben-Menachem Y, Handel SF, Thaggard A, Carnovale RL, Katragadda C, Glass TF. Therapeutic arterial embolization in trauma. *J Trauma* 1979; **19**: 944–52.
112. Panetta T, Sclafani SJA, Goldstein AS, Phillips TF. Percutaneous transcatheter embolisation for arterial trauma. *J Vasc Surg* 1985; **2**: 54–64.
113. Conkle DM, Richie RE, Sawyers JL, Scott HW. Surgical treatment of popliteal artery injuries. *Arch Surg* 1975; **110**: 1351–3.
114. Lim LT, Michuda MS, Flanigan DP, Pankovich A. Popliteal artery trauma. *Arch Surg* 1980; **115**: 1307–13.
115. Flint LM, Richardson JD. Arterial injuries with lower extremity fracture. *Surgery* 1983; **93**: 5–8.
116. Carter SL, McKenzie JG, Hess DR Jr. Blunt trauma to the common femoral artery. *J Trauma* 1981; **21**: 178–9.
117. Welling RE, Kakkasseril J, Cranley JJ. Complete dislocations of the knee with popliteal vascular injury. *J Trauma* 1981; **21**: 450–3.
118. Holleman JH Jr, Killebrew LH. Tibial artery injuries. *Am J Surg* 1982; **144**: 362–4.
119. Mubarak SJ, Owen CA. Double-incision fasciotomy of the leg for decompresion in compartment syndromes. *J Bone Joint Surg* 1977; **59A**: 184–7.

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Review

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Pathophysiology of acute obstructive cholecystitis: implications for non-operative management

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Recent research suggests that disturbances in gallbladder mucosal functions are important in the initiation of acute cholecystitis and its progression. Prostaglandins have pathophysiological significance and prostaglandin synthesis inhibitors such as indomethacin inhibit fluid secretion by gallbladder mucosa, reduce distension and relieve pain. Nerves in the gallbladder wall are involved in disturbed mucosal function, and the benefits of opiates may derive from reduction of active fluid secretion in the inflamed and obstructed gallbladder as well as from central analgesic effects.

Keywords: Acute cholecystitis, animals, intramural nerves, man, opiates, prostaglandins

Early surgery is generally recommended in acute cholecystitis today[1,2], but conservative treatment is still used by many surgeons and insight into the pathophysiology of the acute condition is important. The mechanisms behind the development of acute cholecystitis have been the subject of discussion since the classic work of Aronsohn and Andrews in 1938[3]. The reason why the stone-containing gallbladder suddenly becomes acutely inflamed is unknown, as are the factors that determine the course of this condition. Acute cholecystitis in clinical terms is characterized by abdominal pain and tenderness, rigidity in the right upper quadrant, fever and leucocytosis[4]. Morphologically, the gallbladder is enlarged and exhibits acute inflammatory lesions dominated by invasion of inflammatory cells[4,5]. The functional changes are less well described and will be discussed below.

Initiating events in the development of acute cholecystitis

In acute cholecystitis the cystic duct is usually obstructed by a gallstone and the hydrostatic pressure in the gallbladder lumen is markedly raised[6–8]. Experimental acute cholecystitis may be induced by gallbladder outlet obstruction in combination with intraluminal administration of infectious agents, pancreatic juice, chemical irritants, concentrated bile, lysophosphatidylcholine, a diet inducing lithogenic bile or implantation of gallstones or indwelling catheters[9–15].

Gallbladder obstruction

A prolonged attack of biliary pain after a major meal often precedes clinical signs of acute cholecystitis in humans. The vast majority of cases (95 per cent) involve obstruction of the cystic duct by a gallstone[4]. Postprandial gallbladder contraction and fluid secretion[14] from the mucosa in the stone-containing gallbladder may cause obstruction by impaction of a gallstone in the gallbladder outlet. Obstruction of the human gallbladder, however, does not necessarily lead to acute cholecystitis[4]. Obstructed gallbladders showing no lesions or only discrete inflammatory lesions are commonly seen at elective cholecystectomy. In the experimental situation, ligation of the cystic duct by itself usually does not induce acute cholecystitis[10,11], nor does simple implantation of human gallstones into the gallbladder[12]. The combination of these procedures, however, usually causes severe inflammatory lesions in the gallbladder wall[15].

Luminal factors

Several studies have demonstrated bacterial growth in the biliary tract in 40–60 per cent of cases of acute cholecystitis[16–18]. Bacteria in the gallbladder could promote the inflammatory process, but patients with sterile gallbladder contents exhibit similar morphological signs of acute cholecystitis[4]. Infection seems to be a secondary, additive factor rather than a causative one.

The action of chemical factors such as phospholipase A_2 from liver, gallbladder tissue or pancreatic secretions involves the transformation of the phospholipid to its lyso compound which, because of its cytotoxic properties, has been suggested to be an important factor in the pathogenesis of acute cholecystitis[19,20]. Increased amounts of lysophosphatidylcholine have been demonstrated in hepatic bile and gallbladder contents in patients with acute cholecystitis[19,20]. The gallbladder wall, however, also has the capacity to reacylate lysophosphatidylcholine to lecithin[21], thereby reducing or abolishing its cytotoxic properties[22]. Deconjugated bile salts as well as an altered bile salt composition with a higher proportion of deoxycholate have also been suggested to play a role in the initiation of acute cholecystitis[23,24]. These assumptions seem less likely since bile salts readily disappear from the inflamed gallbladder[25] and the bile acid concentration is low in the obstructed gallbladder[26]. Experimental studies have shown that supersaturated bile, even in the absence of gallstones, will induce acute cholecystitis in the obstructed gallbladder[10]. The contents of the obstructed and inflamed gallbladder may become more saturated due to selective transport of biliary lipids across the wall[14].

Gallbladder mucosal function in acute cholecystitis

The initiated inflammatory response in acute cholecystitis may be maintained or even enhanced by functional responses of the obstructed gallbladder. The raised intraluminal pressure is one

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common denominator and the fact that signs and symptoms usually subside rapidly after simple cholecystostomy emphasizes its pathophysiological importance.

Between meals the gallbladder normally absorbs electrolytes and fluid from its lumen. The gallbladder mucosa also has the ability to secrete fluid[27,28] by an active mechanism that can work against pressure gradients and that is stimulated by prostaglandins[29–31]. In experimental cholecystitis induced by implantation of gallstones[15] or insertion of a chronic indwelling catheter[14] into the obstructed gallbladder or by administration of lysophosphatidylcholine into the gallbladder lumen[9], there is a continuous secretion of fluid into the lumen. This active secretion, which is mediated by intramural nerves in the gallbladder wall[32], is abolished by prostaglandin synthetase inhibitors[13] and is strongly reduced by morphine[33] as well as by peripherally acting opiate agonists such as enkephaline[33] and loperamide[34]. The fluid secretion to the lumen in the inflamed and obstructed gallbladder is enhanced by feeding and reduced by fasting[14]. Acute gallbladder inflammation is seen only in animals that actively secrete fluid to the gallbladder lumen, and there is a relationship between the rate of fluid secretion and the severity of the inflammatory process in laboratory animals[15] and humans[35]. Active fluid secretion in the obstructed gallbladder lumen increases the intraluminal pressure, which may even exceed the arterial blood pressure[8]. A high intraluminal pressure may impair the gallbladder microcirculation and endanger its viability and decrease the clearance of noxious luminal substances[37]. When the intraluminal pressure in the inflamed gallbladder is raised experimentally, the net fluid secretion to the lumen is reduced[15], suggesting that the ongoing active secretion into the gallbladder lumen is balanced by an inhibitory mechanism and/or by retrograde fluid filtration across the epithelium into the capillaries[37]. A recent report suggests a defence mechanism mediated by release of endogenous opiates inhibiting the active mucosal fluid secretion[38].

The role of prostaglandins

The prostaglandin precursor fatty acids are derived from cell membrane phospholipids by the action of phospholipase A_2 and the availability of these fatty acids is a rate limiting factor for prostaglandin synthesis[39]. In addition to membrane-bound phospholipids, the gallbladder stores in its lumen biliary phospholipids, which are synthesized by the liver and contain arachidonic acid[40]. Through the action of phospholipase A_2, lysophosphatidylcholine is released, as well as fatty acids, some of which may serve as generators of prostaglandin synthesis. An increased production of prostaglandins by the inflamed human gallbladder has been demonstrated *in vitro*[41,42] and a recent experimental study demonstrated an increased release *in vivo* of prostaglandin E_2 into the gallbladder lumen in cholecystitis and in response to distension of the normal gallbladder[43].

Exogenous prostaglandin E_2 induces a secretory response by the gallbladder epithelium and contraction of its wall[31]. These effects are mediated by activation of intramural non-adrenergic non-cholinergic nerves[44] and are blocked by opiates[45]. Administration of opiate agonists or inhibition of prostaglandin synthesis blocks fluid secretion by the gallbladder mucosa in experimental cholecystitis[13,33–34] and prostaglandin synthesis inhibition reduces the raised intraluminal pressure in patients with acute cholecystitis[8] and also relieves biliary pain[46], which is thought to be induced by gallbladder distension.

Factors determining the course of acute cholecystitis

An attack of acute cholecystitis usually subsides within one week but may at times progress to gallbladder perforation. Active mucosal fluid secretion raising the hydrostatic pressure in the gallbladder lumen may be one important determinant of the course of the pathophysiological events. The level of the intraluminal hydrostatic pressure is determined by the balance between active fluid secretion into the lumen and filtration of fluid from the lumen to the capillaries[37]. Release of endogenous opiates induced by gallbladder distension[38], or activation of adrenergic mechanisms[47], inhibit the active secretion, thus reducing the intraluminal pressure[37]. The balance between the factors regulating the intraluminal pressure may determine the course of an attack of acute cholecystitis. This is schematically illustrated in *Figure 1*.

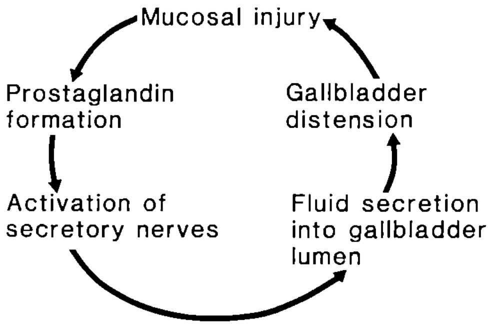
Mucosal injury
Prostaglandin formation
Gallbladder distension
Activation of secretory nerves
Fluid secretion into gallbladder lumen

Figure 1 *Development of acute cholecystitis in the obstructed gallbladder. Mechanical or chemical injury to the gallbladder mucosa increases the formation of prostaglandins which in turn activates mucosal nerves stimulating the epithelial cells to fluid secretion. In the obstructed gallbladder, fluid accumulation distends the gallbladder wall. This distension further enhances prostaglandin formation and a vicious circle is established. Acceleration of the process may be reduced by an inhibition of the active secretion by endogenous opiates and also by an increased transepithelial permeability*

Therapeutic implications

Although the beneficial effects of antibiotics in the conservative management of acute cholecystitis have never been clearly demonstrated, a controlled study has shown that administration of an antibiotic (cefoxitin 2 g t.i.d.) at acute cholecystectomy reduces the rate of postoperative wound infection[49]. In view of the high frequency of bactibilia associated with age[16] and high fever[50], antibiotics may be particularly indicated in such cases.

Conservative treatment should aim at reducing the intraluminal hydrostatic pressure, which is increased by the mucosal fluid secretion[15]. The patient should be kept fasting as this may reduce gallbladder distension by decreasing mucosal fluid secretion[14]. The use of prostaglandin synthesis inhibitors or opiate agonists may reduce fluid secretion[13,33,34], thereby diminishing distension of the obstructed gallbladder. A recent study of patients mainly with *chronic* cholecystitis failed to reveal decreased morphological signs of gallbladder inflammation in response to short-term administration of a prostaglandin synthesis inhibitor[42]. This does not exclude the possibility that inhibition of prostaglandin synthesis or blockade of the effects on gallbladder function of prostaglandins by opiates may favourably affect the course of *acute* gallbladder inflammation. This is supported by the documented ability of prostaglandin synthesis inhibitors to relieve biliary pain[46] and to lower the intraluminal gallbladder pressure in acute cholecystitis[8].

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References

1. Järvinen HJ, Hästbacka J. Early cholecystectomy for acute cholecystitis—A prospective randomized study. *Ann Surg* 1980; **191**: 501–5.
2. Norrby S, Herlin P, Holmin T, Sjödahl R, Tagesson C. Early or delayed cholecystectomy in acute cholecystitis? A clinical trial. *Br J Surg* 1983; **70**: 163–5.

3. Aronsohn HG, Andrews E. Experimental cholecystitis. *Surg Gyn Obstet* 1938; **68**: 748–68.
4. Schein CJ. Acute cholecystitis. New York: Harper and Row, 1972.
5. Edlund Y, Zettergren L. Histopathology of the gall bladder in gallstone disease related to clinical data. With a proposal for uniform surgical and clinical terminology. *Acta Chir Scand* 1958/1959; **116**: 450–60.
6. Shefer VF. Pressure in the gall bladder cavity in acute cholecystitis. *Vrach Delo* 1977; **4**: 22–5.
7. Csendes A, Sepulveda A. Intraluminal gall bladder pressure measurements in patients with chronic or acute cholecystitis. *Am J Surg* 1980; **139**: 383–4.
8. Thornell E, Jansson R, Svanvik J. Indomethacin reduces raised intraluminal gall bladder pressure in acute cholecystitis. *Acta Chir Scand* 1985; **151**: 261–5.
9. Neiderhiser D, Thornell E, Björck S, Svanvik J. The effect of lysophosphatidylcholine on gallbladder function in the cat. *J Lab Clin Med* 1983; **101**: 699–707.
10. Morris CR, Hohf RP, Ivy AC. An experimental study of the role of stasis in the etiology of cholecystitis. *Surgery* 1952; **32**: 673–85.
11. Roslyn JJ, Den Besten L, Thompson JE, Silverman BF. Roles of lithogenic bile and cystic duct occlusion in the pathogenesis of acute cholecystitis. *Am J Surg* 1980; **140**: 126–30.
12. Schein CJ, Rosen RG, Warren A, Gliedman ML. A vagal factor in cholecystitis. *Surgery* 1969; **66**: 345–52.
13. Svanvik J, Thornell E. Zettergren L. Gall bladder function in experimental cholecystitis: reversal of the inflammatory net fluid 'secretion' into the gall bladder by indomethacin. *Surgery* 1981; **89**: 500–6.
14. Svanvik J, Allen B, Pellegrini C, Bernhoft R, Way L. Transport of fluid and biliary lipids in the canine gall bladder in experimental cholecystitis. *J Surg Res* 1986; **41**: 425–31.
15. Jivegård K, Rådberg G, Wahlin T. An experimental study on the role of gall bladder mucosal fluid secretion and intraluminal pressure in cholecystitis. *Acta Chir Scand* 1986; **152**: 605–10.
16. Edlund Y, Mollstedt BO, Ouchterlony Ö. Bacteriological investigation of the biliary system and liver in biliary tract disease correlated to clinical data and microstructure of the gall bladder and liver. *Acta Chir Scand* 1958/1959; **116**: 461–76.
17. Bergan T, Dobloug I, Linvåg I. Bacterial isolates in cholecystitis and cholelithiasis. *Scand J Gastroent* 1979; 625–31.
18. Truedson H, Elmros T, Holm S. The incidence of bacteria in gall bladder bile at acute and elective cholecystectomy. *Acta Chir Scand* 1983; **149**; 307–13.
19. Gottfries A, Nilsson S, Samuelsson B, Scherstén T. Phospholipids in human hepatic bile, gall bladder bile, and plasma in cases with acute cholecystitis. *Scand J Clin Lab Invest* 1968; **21**: 168–76.
20. Sjödahl R, Wetterfors J. Lysolecithin and lecithin in gall bladder wall and bile; their possible roles in the pathogenesis of acute cholecystitis. *Scand J Gastroent* 1974; **9**: 519–25.
21. Neiderhiser DH, Morningstar WA, Roth HP. Absorption of lecithin and lysolecithin by the gall bladder. *J Lab Clin Med* 1973; **82**: 891–7.
22. Gjone E. Inhibitory actions of serum lecithin on the hemolytic activity of serum lysolecithin *in vitro*. *Scand J Clin Lab Invest* 1961; **13**: 369–73.
23. Tera H. The concentrating activity of the normal human gall bladder measured by direct bile analyses *in vivo*. *Acta Chir Scand* 1961; **122**: 402.
24. Heuman R, Norrby S, Sjödahl R, Tiselius HG, Tagesson C. Altered gall bladder bile composition in gallstone disease. Relation to gallbladder wall permeability. *Scand J Gastroent* 1980; **15**: 581–6.
25. Ostrow JD. Absorption by the gall bladder of bile salts, sulfobromophthalein and iodioamide. *J Lab Clin Med* 1969; **74**: 482–94.
26. Rådberg G, Zettergren L, Jivegård L, Svanvik J. Biliary lipids and bilirubin in gall bladder contents and hepatic bile related to morphology in the gall bladder wall in patients with cholecystolithiasis. Submitted.
27. Schafer DE, Nicoloff DM, Gleason DF, Carlsson TJ. Gall bladder secretion induced by an enterotoxin-like fraction of crude v. cholerae supernatant. *Gastroenterology* 1969; **56**: 1195.
28. Jansson R, Steen G, Svanvik J. Effects of intravenous vasoactive intestinal polypeptide (VIP) on gall bladder function in the cat. *Gastroenterology* 1978; **75**: 47–50.
29. Heintze K, Göetz R, Koerlings H, Wood J. Characterization of the prostaglandin induced secretion in the isolated gall bladder of guinea pig. *Naunyn Schmiedeberg's Arch Pharmacol* 1976; 292–3: R34.
30. Heintze K, Leinesser W, Petersen KU, Heidenreich O. Triphasic effect of prostaglandins E_1, E_2 and F_2 on the fluid transport of isolated gall bladder of guinea-pig. *Prostaglandins* 1975; **9**: 309–22.
31. Thornell E, Svanvik J, Wood JR. Effects of intraarterial prostaglandin E_2 on gall bladder fluid transport, motility and hepatic outflow in the cat. *Scand J Gastroent* 1981; **16**: 1083–8.
32. Jivegård L, Thornell E, Svanvik J. Gallbladder inflammatory fluid secretion in experimental cholecystitis is influenced by intramural nerves. *Dig Dis Sci* 1987, in press.
33. Jivegåard L, Thornell E, Björck S, Svanvik J. The effects of morphine and enkephalin on gall bladder function in experimental cholecystitis. Inhibition of inflammatory gall bladder secretion. *Scand J Gastroent* 1985; **20**: 1049–56.
34. Jivegård L, Svanvik J. Loperamide inhibits gallbladder inflammatory fluid secretion in experimental cholecystitis. *Naunyn-Schmiedeberg's Arch Pharmacol* 1986; **333**: 178–81.
35. Nahrwold D, Rose R, Ward S. Abnormalities in gallbladder morphology and function in patients with cholelithiasis. *Ann Surg* 1976; **184**: 415–21.
36. Thornell E. Effects of raised intraluminal pressure on gall bladder function and hepatic bile outflow in the cat. *Scand J Gastroent* 1981; **16**: 873–7.
37. Jivegård L. Prostaglandins, opioids and intramural nerves in the function of the normal and inflamed gall bladder. An experimental study in the cat. PhD Thesis, University of Göteborg, Göteborg, Sweden, 1986.
38. Jivegard L, Thune A, Svanvik J. Endogenous opioids depress mucosal fluid secretion in the inflamed and distended feline gallbladder in the anesthetized cat (abstract). *Gastroenterology* 1987: in press.
39. Bartels J, Kunze H, Vogt W, Wille G. Prostaglandin: Liberation from and formation in perfused frog intestine. *Naunyn-Schmiedeberg's Arch Pharmacol* 1970; **266**: 199–207.
40. Ahlberg J, Curstedt T, Einarsson K, Sjövall J. Molecular species of biliary phosphatidylcholines in gallstone patients: the influence of treatment with cholic acid and chenodeoxycholic acid. *J Lipid Res* 1981; **22**: 404–8.
41. Wood JR, Stamford IF. Prostaglandins in chronic cholecystitis. *Prostaglandins* 1977; **13**: 97–107.
42. Kaminsky DL, Deshpande Y, Thomas L, Qualy J, Blank W. Effect of oral ibuprofen on formation of prostaglandins E and F by human gall bladder muscle and mucosa. *Dig Dis Sci* 1985; **30**: 933–40.
43. Thornell E, Jivegård L, Bukhave K, Rask-Madsen J, Svanvik J. Prostaglandin E_2 formation by the gall bladder in experimental cholecystitis. *Gut* 1986; **27**: 370–3.
44. Jivegård L, Svanvik J. Intraluminal prostaglandin E_2 affects gallbladder function by activation of intramural nerves in the anaesthetized cat. *Acta Physiol Scand* (in press).
45. Jivegård L, Svanvik J. The influence of morphine, loperamide and naloxone on gall bladder response to prostaglandin E_2 in the anesthetized cat. *Acta Physiol Scand* 1986; **127**: 275–9.
46. Thornell E, Jansson R, Svanvik J. Indomethacin intravenously, a new way for effective relief of biliary pain; a double blind study in man. *Surgery* 1981; **90**: 468–72.
47. Jivegård L. Svanvik J. Adrenergic influence on gallbladder function in experimental cholecystitis. *Scand J Gastroenterol* 1986; **128**: 639–42.
48. Thornell E. Mechanisms in the development of acute cholecystitis and biliary pain. *Scand J Gastroenterol* 1982; suppl 76.
49. Lahtinen J, Alhava EM, Katila ML, Pääkkönen M. Prophylactic antibiotics for acute cholecystitis treated by early surgery. A double blind controlled trial. *Proc. 13th Int. Congress of Chemotherapy*, Vienna 1983; sect 7, part 68, 28–32.
50. Claesson B. Microflora of the biliary tract and liver—clinical correlates. *Dig Dis* 1986; **4**: 93–118.

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Endoscopic biliary drainage

Endoscopic biliary drainage (EBD) has become an established method of relieving posthepatic jaundice. This study comprises 399 patients in whom 472 EBD procedures were performed during a 5 year period; 272 patients had malignant obstruction, 36 had a benign stricture, 79 had common duct stones and 12 patients had other benign conditions requiring drainage. A 7F double pigtail endoprosthesis was used in the majority of patients and was inserted with an Olympus JF-1T duodenoscope. Ninety-two per cent of the prostheses were correctly positioned, and 88 per cent of these functioned well with relief of symptoms. The 30-day mortality was 22 per cent and one-third of these deaths were due to the procedure, septicaemia being the dominant hazard. This was more marked if the obstruction was not relieved satisfactorily. Antibiotic cover was not used routinely and had not been prescribed in any of the fatal cases. This omission probably made a significant contribution to the septicaemia. Acute pancreatitis and haemorrhage were rare complications and both were probably related to the coincidental sphincterotomy. Prostheses intended for permanent relief of malignant obstruction remained patent for 2–3 months (median) with a wide range of 1–618 days. Survival among these patients is so short, that one or two EBD procedures will keep the majority of patients free from symptoms related to biliary obstruction, and only two patients needed more than three procedures. Fifty-one patients with pancreatic head carcinoma had EBD as a bypass before an intended operation. Only 16 patients actually had a resection. The median survival among the 51 patients was 106 days (compared with 59 days among 100 patients with a permanent prosthetic bypass). Only one patient with a very small periampullary carcinoma has survived for more than 3 years. Forty-seven patients are dead. Among the 51 patients in whom radical resection was intended two-thirds were actually treated by permanent surgical or prosthetic bypass.

Keywords: Bile duct obstruction, endoscopic retrograde cholangiopancreaticography, drainage, prosthesis

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Endoscopic biliary drainage (EBD) in combination with diagnostic endoscopic retrograde cholangiopancreaticography (ERCP) was introduced relatively recently[1,2]. An internal prosthesis placed through an obstruction due to malignancy, benign stricture or gallstones now allows bilio-enteric drainage, with relief of jaundice and improved hepatic function[3]. This method provides an alternative to the method of percutaneous transhepatic biliary drainage (PTBD) described in 1974[4]. In several studies, external and internal drainage of the obstructed biliary tract through the transhepatic approach has been successfully accomplished, but the method has serious side effects, notably bile leakage and haemorrhage from the puncture site. Puncture-free application of stents as in EBD is therefore an attractive alternative.

EBD has been performed at our Unit since 1973, almost exclusively by two endoscopists with experience of more than 2000 diagnostic and therapeutic ERCP procedures.

Patients and methods

This report presents the results of our experience with EBD in 399 consecutive patients treated from November 1980 to September 1985. There were 223 females and 176 males with a median age of 73 years (range 11–93 years); 95 per cent of the patients were 38–90 years old. Four hundred and seventy-two examinations and drainage procedures were performed. Sixty-one patients were inpatients in our hospital. The remaining 338 patients were admitted as outpatients from other hospitals on the day of examination and returned to their own hospital shortly after EBD. A follow-up was made not less than 16 months after EBD.

The indications for ERCP and EBD were jaundice (381), pain (88), cholangitis (49) and postoperative bile leak (2). The nature, site and size of the obstructing lesion was demonstrated by ultrasound scanning and ERCP. A tissue diagnosis was obtained in 83 of 181 patients with pancreatic head carcinoma, in all 11 cases of periampullary carcinoma, in 30 of 39 patients with obstruction from extrabiliary metastases and in 18 of the 41 patients with cholangiocarcinoma. The remaining diagnoses were based upon the typical ultrasound or cholangiographic appearance of bile duct or pancreatic tumours. All diagnoses are shown in *Table 1*.

Four hundred and seventy examinations were performed under sedation with diazepam. Premedication was with atropine and pethidine. Two examinations were performed under general anaesthesia. Coagulation ability was monitored and deficiencies corrected before the procedure. Antibiotics (penicillin and streptomycin) were given to patients showing signs of biliary tract infection, but were not given routinely to all patients. If free drainage of all parts of the obstructed biliary ductal system was not obtained we always recommended antibiotic cover, and prompt alternative drainage by PTBD or operative bypass. This was intended to prevent sepsis, especially if contrast had been injected into the bile tree above the obstruction.

The vast majority of the procedures were performed with an Olympus JF-1T duodenoscope with biopsy channel 2·8 mm, and as a routine a 7F double pigtail Teflon prosthesis (W. Cook Europe, Copenhagen, Denmark) of suitable length to allow the proximal tip to lie well above the stenosis was inserted. The prosthesis was applied over a Teflon-coated guidewire according to the technique described by

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Table 1 *Success rate in endoscopic biliary drainage in terms of insertion and immediate function*

Diagnosis	*n*	Success on first attempt	Success on second attempt	Total
Pancreatic head carcinoma	181	143 (79%)	17 (9%)	160 (88%)
Hilar cholangiocarcinoma	21	18 (86%)	2 (10%)	20 (95%)
Low cholangiocarcinoma	14	11 (79%)	1 (7%)	12 (86%)
Hilar and low cholangiocarcinoma	6	3 (50%)	1 (17%)	4 (67%)
Periampullary carcinoma	11	11 (100%)	—	11 (100%)
Metastases from lesions elsewhere	39	35 (90%)	—	35 (90%)
Benign stricture	36	33 (92%)	—	33 (92%)
Common duct stones	79	78 (99%)	—	78 (99%)
Other	12	12 (100%)	—	12 (100%)
Total	399	344 (86%)	21 (5%)	365 (92%)

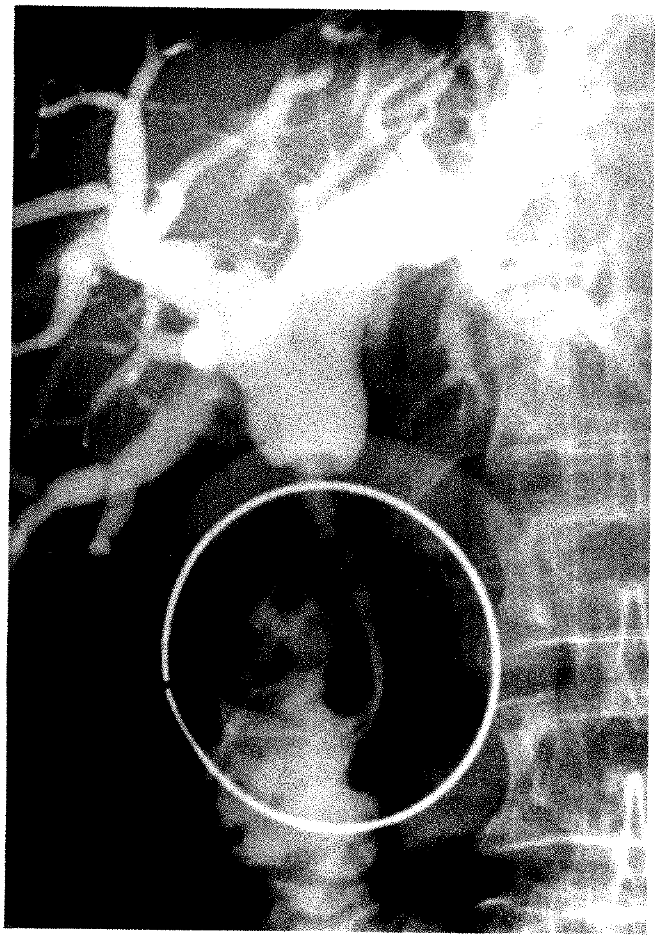

Figure 1 *Two endoprostheses inserted across an obstructing pancreatic head carcinoma with bile discharge into the duodenum*

Soehendra and Beynders-Frederix[2]. New prostheses and duodenoscopes appeared during the period and a change in technique was a natural consequence. Two or three prostheses were inserted with increasing frequency to extend the period of patency, allowing bile to flow in the space between the prostheses as well as through them. With the recent development of large calibre (3·2 mm) endoprostheses[5] and new types of duodenoscopes with a 3·7 mm biopsy channel, these types of prostheses were often chosen.

In hilar tumours an attempt was always made to drain each lobe separately leaving no part of the biliary tree obstructed. Sixteen patients with non-extractable common duct stones had nasobiliary drainage for infusion of bile acids for dissolution of stones. One patient with sepsis from an obstructing malignant lymphoma was also treated by nasobiliary drainage. Three of the seventeen patients had an endoprosthesis as well to ensure free bile flow in the event of dislocation of the nasobiliary tube.

A sphincterotomy always preceded the procedure when two or more conventional prostheses were used or when large bore prostheses were inserted. Sphincterotomy was not used routinely with single 7F prostheses, unless common duct stones were removed on the same occasion.

The patients were allowed to eat later in the day and no specific precautions were taken, unless complications were noted. A repeat EBD was always performed in case of recurrence, with replacement of obstructed prostheses or insertion of further prostheses.

Five patients had been operated on by a Billroth II resection on an earlier occasion.

All five had a successful endoscopic drainage.

Endoprosthesis function

Correct positioning of the prosthesis was assumed if there was prompt discharge of bile from the prosthesis and the position was verified by an abdominal radiograph showing the prosthesis in the correct position. An example is shown in *Figure 1*. The prosthesis was considered to be functioning well if bilirubin levels became normal and alkaline phosphatase levels in serum declined within a few days of the EBD, and if at the same time the symptoms were relieved. Recurrent jaundice or cholangitis were considered to be signs of a non-functioning or displaced prosthesis.

Thirty days mortality was recorded and 95 per cent confidence limits are used in reporting data.

In 254 patients, EBD was intended as definitive treatment for relief of symptoms. Of these patients 67 had non-resectable malignant obstruction and 187 were too old for an operation. One hundred and eighteen patients had EBD as a preliminary drainage procedure preoperatively. The remaining 27 patients had a prosthesis inserted for other reasons, notably non-extractable common duct stones and refusal to have operation.

Results

The results from the first drainage in the 399 patients are set out in *Table 1*. Three hundred and forty-four patients had a prosthesis inserted successfully on the first occasion and in an additional 22 patients success was achieved at the second attempt, a success rate of 92 per cent.

The observation period was too short to assess the function of the prosthesis in 65 patients. Of the 301 patients left for observation, 266 (88 per cent) had a well-functioning prosthesis according to the above criteria. Thirty-five patients did not benefit from biliary drainage. Too few patients had two or more prostheses inserted to allow conclusions as to whether or not they had improved drainage.

Complications

Eighty-seven patients died within 30 days of EBD (22 per cent).

Thirty-five patients (9 per cent) died as a consequence of the procedure. Nineteen of them died from septicaemia. Eleven patients had pyrexia with no other signs of sepsis, negative blood cultures, and no signs of infection of parenchymatous organs. They died after a rapid deterioration in their general condition. Two patients died from severe pancreatitis. One patient died from cardiac failure after uneventful EBD. Another patient died from peritonitis shortly after EBD. Post-mortem examination disclosed no signs of perforation of the biliary tree; although no firm diagnosis was obtained it must be

Table 2 *Time from first drainage with well-functioning prosthesis to death in 140 patients with malignant bile duct obstruction in whom permanent endoscopic drainage was intended*

Diagnosis	*n*	Median survival (days)	Range (days)	95% of patients living (days)	25% dead in less than (days)	25% alive for more than (days)
Pancreatic head carcinoma	100	59	2–712	6–447	18	141
Cholangiocarcinoma	20	89	10–1188	—	34	341
Metastases from lesion elsewhere	20	62	3–396	—	44	132

Table 3 *Patency of prosthesis (days) among patients with repeated EBD procedures*

	n	Median (days)	Range (days)	25% occluded in less than (days)	25% patent for more than (days)
First prosthesis	45	49	1–618	12	160
Second prosthesis	42	76	1–451	38	164
Third prosthesis	10	48	7–180	—	—

presumed that peritonitis was a consequence of the EBD. The last patient died as a result of misinterpretation in that ERCP suggested a pancreatic head carcinoma. After uneventful EBD this patient died from complications following pancreatic head resection. Post-mortem examination concluded that a benign duodenal ulcer had been the cause of the radiographic pattern.

Fifty-two deaths were considered to be unrelated to EBD: extended cancer (44), haemorrhage following PTBD after an unsuccessful attempt at EBD (2), complications of surgery (4); no information was obtained about the deaths of the remaining 2 patients.

Septicaemia was the main hazard in this series. Thirty-one patients had clinical signs of sepsis and nineteen of them also had positive blood cultures. Seventy-five other patients had fever with a temperature above 38·5°C. None of the patients with sepsis had received any antibiotics before or immediately after the procedure.

An elevated serum amylase level was encountered in 41 patients in the first days following EBD, but was considered a harmless reaction from the procedure unless clinical symptoms suggested the presence of pancreatitis. Three patients were considered clinically to have pancreatitis and two of them died with severe pancreatitis. Both had a coincidental sphincterotomy. These were the only two cases of serious pancreatitis in the series.

Two patients bled after EBD with sphincterotomy. One of them had an operation; the other patient had a transfusion of 1 unit of blood during preparation for surgery, but then the haemorrhage stopped spontaneously. There were no deaths due to bleeding in this series.

The function of the prostheses was assessable in 17 patients who died within 30 days of EBD, and whose death was regarded as a consequence of EBD. Seven of 35 (20 per cent) who had a non-functioning prosthesis died (95 per cent confidence limits 8–37 per cent) compared with only 10 patients out of 266 (4 per cent) with a well-functioning prosthesis (95 per cent confidence limits 1–7 per cent). This difference is significant ($P<0\cdot05$). While all of the patients had a correctly inserted prosthesis, it is essential to obtain unimpeded bile flow once contrast has been injected.

The prostheses were displaced from the biliary tree in four patients. This caused no harm. In another three cases the proximal tip of the bent prosthesis was seen penetrating the common bile duct into the hepatoduodenal ligament (two patients) or penetrating the cystic duct into the peritoneal cavity (one patient) at subsequent operation. The patients had no sign of perforation pre-operatively. We have abandoned short prostheses and recommend the use of prostheses long enough to allow the proximal tip to be placed in the intrahepatic part of the biliary tree, where perforation would probably be harmless.

Late prosthesis function

One hundred and forty patients with permanent, palliative drainage had a well-functioning prosthesis initially. However, forty-five patients had to have their prostheses replaced or supplemented to maintain this function. Many of the patients had coincidental sphincterotomy, and the result therefore reflects the combined effect of a patent prosthesis and the relief caused by the sphincterotomy. The survival of the patients is shown in *Table 2*.

Most of the 140 patients with intended permanent prosthetic drainage died before their prostheses blocked. Forty-five patients had their prostheses replaced or new ones added on one or more occasions. They enabled us to assess the duration of prosthesis patency (*Table 3*).

Two patients with cholangiocarcinoma found unresectable at exploratory laparotomy had the prostheses renewed five and six times respectively. They survived 492 and 1188 days after the initial drainage with an acceptable quality of life apart from the episodes when the prostheses were occluded.

Fifty-one patients with potentially resectable pancreatic head carcinoma had a preliminary drainage if ultrasound and CT scanning indicated resectability. Only 16 patients actually had a resection; 25 were found unresectable and 10 deteriorated so rapidly that the thought of operation was abandoned. Four of the fifty-one patients are still alive, one of them 42 months after a Whipple's procedure while three patients are alive 1–2 years after radical resection (one patient) or a palliative procedure (two patients). Forty-seven patients are dead. Their median survival was 106 days (range 8–1041 days); 25 per cent lived for less than 16 days and 25 per cent for more than 240 days.

Discussion

Resection for pancreatic head carcinoma in jaundiced patients can carry a very high operative risk with a 30-day mortality of 20 per cent[6–8] and a considerable morbidity rate[9]. Bypass operations for their part are far from harmless particularly in old and severely ill patients[10]. The prognosis even after radical resection is very poor, with a 10 per cent overall survival rate at 2 years. For cholangiocarcinoma the figures are equally bad[8]. Alternative non-operative drainage procedures have therefore aroused much interest. The first method available was PTBD and this allowed external tubes and often internal prostheses to be placed in the biliary tree[11]. This resulted in relief of jaundice and cholangitis which was as prompt and effective as after surgical bypass. However, it unfortunately carried many serious hazards relating to the transhepatic route, notably haemorrhage and bile leakage from the puncture site[7,12,13].

EBD was introduced as an alternative to PTBD. The internal prosthesis allowed bile to re-enter the bowel and offered a more attractive physiological alternative than external transhepatic drainage. Furthermore, it is much more appealing and comfortable for the patient. Our results show that, provided EBD is carried out by a skilled endoscopist, it carries a high success rate with 92 per cent of prostheses correctly placed. These results compare favourably with most results of PTBD using internal stents[7,13–15]. However, the technique is difficult and time consuming to learn. This is obvious from our experience with insertion of endoprostheses in patients with pancreatic head carcinoma. Among the first 60 patients the success rate was 82 per cent rising to 95 per cent among the last 60 patients included in the study.

The endoscopic approach avoids the main hazards of PTBD[16] but still inolves a considerable risk of sepsis, as do all types of invasive biliary procedures[17]. Sepsis carried the main responsibility for the fatal cases referred to in this report, in which omission of antibiotic cover must be implicated. Sepsis as a consequence of contamination from the endoscope is less likely because sepsis was much more frequent in the group where insertion of the prostheses failed. Blood cultures were not always obtained before antibiotics were administered but, in the light of our experience, we now recommend the use of antibiotics active against the most common types of bacteria isolated from infected bile, namely *Klebsiella*, *Escherichia coli*, *Pseudomonas* and *Streptococcus faecalis*[17]. It is also essential to relieve the obstructed biliary tree by PTBD or operation immediately if EBD drainage fails.

The use of pre-operative biliary drainage is controversial. Many studies have failed to demonstrate any advantage. This may be due to the many risks related to PTBD which may mask any advantages. If ERCP is used for pre-operative examination of jaundiced patients, EBD is, in our view, an essential part of the examination[7,13,14,18].

Operations for common duct stones carry high risks in old people[19,20] and an internal prosthesis is a valuable adjunct to sphincterotomy if all stones cannot be removed because of large size or a duct stricture. A prosthesis in the common duct then prevents cholangitis from impacting stones[21].

The frequency of significant acute pancreatitis after EBD among patients in this study was surprisingly low. The two patients who died from acute pancreatitis also had a sphincterotomy. Pancreatitis is a complication of ERCP with sphincterotomy in 1–2 per cent of cases[22], and we consider it likely that the sphincterotomy was responsible for the fatal outcome rather than the insertion of a prosthesis. In fact, we would have expected pancreatitis to occur if no sphincterotomy was added, because occlusion of the pancreatic duct might be expected to generate acute pancreatitis. When only one 7F prosthesis is inserted we have no reluctance in omitting sphincterotomy, unless common duct stones are to be removed.

The median period of prosthesis patency in patients treated by permanent bilio-enteric bypass is a few months although there is a great range. These results are comparable to those obtained with permanent PTBD[12,14,15,17]. It is probable that the 10F endoprostheses now available[5] will remain patent for a longer period.

The vast majority of our patients with permanent prostheses only needed one EBD because of their short survival. Some had two and a few had three EBD procedures. Only two patients had the prosthesis replaced more than three times. This seems an attractive alternative to operative bypass and in one recent study, EBD was shown to be equally efficient and followed by fewer major complications and shorter hospital stay than surgical bypass[10].

References

1. Laurence BH, Cotton PB. Decompression of malignant biliary obstruction by duodenoscopic intubation of bile ducts. *Br Med J* 1980; **280**: 522–3.
2. Soehendra N, Beynders-Frederix V. Palliative Gallengandrainage. *Dtsch Med Wochenschr* 1979; **104**: 2–3.
3. Rokkjaer M, Kruse A. Endoscopic bile duct drainage in cases of malignant obstructive jaundice. *Ugeskr Laeger* 1984; **146**: 1126–9.
4. Molnar W, Stockun E. Relief of obstructive jaundice through percutaneous transhepatic catheter; a new therapeutic method. *Am J Roentgenol* 1974; **122**: 356–67.
5. Huibregtse K, Tytgat GN. Palliative treatment of obstructive jaundice by transpapillary introduction of large bore bile duct endoprosthesis. *Gut* 1982; **23**: 371–5.
6. Grace PA, Pitt HA, Longmire WP. Pancreatoduodenectomy with pylorus preservation for adenocarcinoma of the head of the pancreas. *Br J Surg* 1986; **73**: 647–50.
7. McPherson GAD, Benjamin IS, Hogdson HJF, Bowley NB, Allison DJ, Blumgart LH. Pre-operative percutaneous transhepatic biliary drainage: the results of a controlled trial. *Br J Surg* 1984; **71**: 371–5.
8. Benjamin IS. Tumour and host. Aims and decisions in pancreatic cancer. In: *Pancreatic Cancer*. Geneva: UICC, 1981: 103–13.
9. Sonnenfeld T, Gabrielsson N, Granquist S, Perbeck L. Non-resectable malignant bile duct obstruction. *Acta Chir Scand* 1986; **152**: 297–300.
10. *Pancreatic Cancer: UICC Technical Report Series 57*. International Union Against Cancer: Geneva: UICC, 1981.
11. Bornman PC, Harries-Jones EP, Tobias R, Van Stiegmann G, Terblanche J. Prospective controlled trial of transhepatic biliary endoprosthesis versus bypass surgery for incurable carcinoma of head of pancreas. *Lancet* 1986; **i**: 69–71.
12. Dooley JS, Dick R, George P, Kirk RM, Hobbs KEF, Sherlock S. Percutaneous transhepatic endoprosthesis for bile duct obstruction. *Gastroenterology* 1984; **86**: 905–9.
13. Pitt HA, Gomes AS, Lois JF, Mann LL, Deutsch LS, Longmire WP. Does preoperative percutaneous biliary drainage reduce operative risk or increase hospital cost? *Ann Surg* 1985; **201**: 545–52.
14. Hansson JA, Hoevels J, Simert G, Tylén U, Vang J. Clinical aspects of nonsurgical percutaneous transhepatic bile drainage in obstructive lesions of the extrahepatic bile ducts. *Ann Surg* 1979; **189**: 58–61.
15. Nilsson U, Evander A, Ihse I, Lunderquist A, Mocibob A. Percutaneous transhepatic cholangiography and drainage. *Acta Radiol* 1983; **24**: 433–9.
16. Speer AG, Cotton PB, Hatfield A *et al.* Randomised trial comparing endoscopic and percutaneous prostheses in poor risk patients with malignant obstructive jaundice. *Gut* 1985; **26**: A1135.
17. Keighley MRB. Microorganisms in the bile. *Ann R Coll Surg Engl* 1977; **59**: 329–34.
18. Burcharth F, Efsen F, Christiansen LA *et al.* Nonsurgical internal biliary drainage by endoprosthesis. *Surg Gynecol Obstet* 1981; **153**: 857–60.
19. McSherry CK. Cholecystectomy and common duct exploration. In: Blumgart LH, ed. *The Biliary Tract*. London, Edinburgh, Melbourne, New York: Churchill Livingstone, 1982; 128–42.
20. Thompson MH. Influence of endoscopic papillotomy on the management of bile duct stones. *Br J Surg* 1986; **73**: 779–81.
21. Lygidakis NJ, Brummelkamp WH. Bacteremia in relation to intrabiliary pressure in proximal v. distal malignant biliary obstruction. *Acta Chir Scand* 1986; **152**: 305–7.
22. Sarr MG, Fishman EK, Milligan FD, Siegelmann SS, Cameron JL. Pancreatitis or duodenal perforation after peri-Vaterian therapeutic endoscopic procedures: diagnosis, differentiation and management. *Surgery* 1986; **100**: 461–6.

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Reticulo-endothelial function in obstructive jaundice

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A study of reticulo-endothelial function was performed in 30 patients with obstructive jaundice. Reticulo-endothelial phagocytic function, measured by the clearance of intravenous human micro-aggregated albumin, was significantly depressed in jaundiced patients compared with non-jaundiced controls ($P<0{\cdot}001$)*. There was a significant correlation* ($P<0{\cdot}001$) *between phagocytic function and plasma bilirubin level but not with transaminase or bile salt level. Phagocytic function was not related to the presence of malignancy, but was markedly reduced in patients with cholangitis. There was no reduction in hepatic sinusoidal blood flow, opsonin levels (fibronectin, IgG, complement) or serum opsonic activity to account for the reticulo-endothelial dysfunction.*

Keywords: Reticulo-endothelial system, phagocytosis, endotoxin, extrahepatic bile duct obstruction, cholestasis, Kupffer cell, fibronectin, bilirubin, opsonin

Renal impairment is common in patients with obstructive jaundice and is associated with the presence of circulating systemic endotoxins[1,2]. Two main factors are believed to predispose to systemic endotoxaemia: increased endotoxin absorption from the gut into the portal vein[1] and depressed hepatic reticulo-endothelial function allowing 'spillover' of endotoxins into the systemic circulation[3]. Reticulo-endothelial function is depressed pre-operatively in nearly 50 per cent of patients with obstructive jaundice[4]. The aetiology of this depression is unknown but, since the hepatic Kupffer cells manifest 80–90 per cent of the total reticulo-endothelial activity[5], it can be inferred that either a direct or indirect depressed of Kupffer cell function occurs in obstructive jaundice.

Possible causative factors for depression of Kupffer cell function in obstructive jaundice include a reduction in opsonin levels or activity, an alteration in hepatic sinusoidal blood flow, or a direct depression of Kupffer cells. In order to investigate some of these factors reticulo-endothelial function has been studied in a group of patients with obstructive jaundice.

Patients and methods

Thirty patients with obstructive jaundice (plasma bilirubin > 30 μmol/l) were studied. There were 13 women and 17 men with a mean age of 72 years (range 57–91). The causes of obstructive jaundice are shown in *Table 1*. Cholangitis defined as the presence of fever (> 38°C) and rigors or abdominal pain/tenderness, in jaundiced patients, and where no other site of infection was apparent, occurred in five of these patients. Ten non-jaundiced patients (mean age 70) acted as controls for the hepatic sinusoidal blood flow measurements and reticulo-endothelial phagocytic test, and 25 non-jaundiced patients (mean age 62) acted as controls for the plasma fibronectin levels.

Radiolabelled human micro-aggregated albumin

Micro-aggregated albumin was prepared by a method described previously[6] which requires a 3 per cent ^{125}I-radiolabelled albumin suspension to be heated and agitated until the albumin molecules form aggregates measuring 10–30 nm in size. Patients were given 2 ml Lugol's iodine orally or a 5 ml Lugol's iodine injection (St. George's Hospital Pharmacy, Tooting, London, UK) before each test to prevent thyroidal uptake of free radioactive iodine.

There is a critical dose of intravenous micro-aggregated albumin injection below which the rate of clearance is constant and independent of the amount injected. Such low doses can be used to measure hepatic sinusoidal blood flow[7,8]. Four healthy subjects were injected with 0·1 mg, 0·25 mg and 0·5 mg micro-aggregated albumin/kg body weight, each dose being given on separate days. Half-life clearances of the three doses of albumin were similar in each patient indicating that the critical dose had not been exceeded. In order to measure the hepatic sinusoidal blood flow in the patients studied, 0·5 mg micro-aggregated albumin/kg body weight was injected intravenously into an antecubital fossa vein. Venous samples of 5 ml were removed from the contralateral arm at 0 (to check for background radiation), 3, 4, 5, 6 and 8 min and put into EDTA-containing tubes. One millilitre plasma samples were counted on a LKB Wallac 80 000 gamma counter for 2 min. Clearance half-lives were calculated using a non-linear regression computer program (Nonlin, Surrey University). In order to measure reticulo-endothelial phagocytosis, patients were injected with 5 mg micro-aggregated albumin/kg body weight into an antecubital fossa vein at least 40 min after the hepatic sinusoidal blood flow test. Blood samples were taken at 0, 3, 6, 9, 12 and 15 min, and half-life clearances were calculated as for the hepatic sinusoidal blood flow test.

Serum bile salts

Total fasting serum bile salt levels were measured according to the principle described by Mashige *et al.*[9] and Osuga *et al.*[10] using the reagent kit, Enzabile (Nyegaard Diagnostica, Norway). In 15 non-jaundiced subjects the levels of total serum bile salts were found to range from 2·4 to 5·4 μg/ml.

Opsonin assays

Blood taken for fibronectin assay was added to tubes containing 3·13 per cent sodium citrate (Laboratory Sales), 1:9 volumes blood. All specimens were separated within 3 h and the plasma was stored at −30°C before assay. Fibronectin was measured by a kinetic immunoturbidimetric assay (Boehringer Mannheim Biochem). IgG was measured using a standard automated immunoturbidimetric method. The following complement components were measured by an automated immunoturbidimetric assay: C3, C4, β1H and factor B.

Opsonic activity

Serum opsonic activity was measured using a modification of the method described by Kerr *et al.*[11]. The basis of the test is to measure the phagocytosis of fluoresceinated yeast by isolated polymorphonuclear leucocytes and monocytes in the presence of the serum to be tested. Phagocytosis can be quantitated fluorimetrically because phagocytosed yeast within white cells will continue to fluoresce, while the fluorescence of yeast not phagocytosed can be abolished by the addition of crystal violet. All samples were measured in duplicate, and results are expressed as a percentage compared to a pooled reference sample of 20 healthy subjects.

Table 1 *Diagnoses in patients with obstructive jaundice*

Carcinoma of pancreas	13
Carcinoma of bile ducts	1
Carcinoma of gallbladder	1
Porta hepatis metastasis	1
Choledocholithiasis	9
Choledocholithiasis + cholangitis	5

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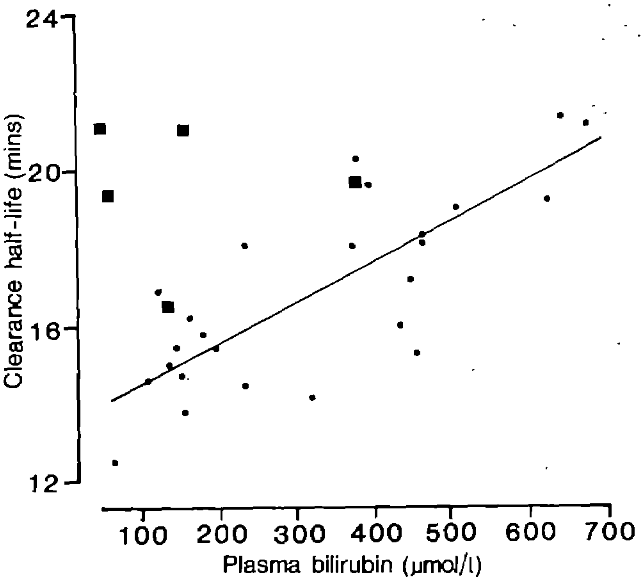

Figure 1 *Correlation of micro-aggregated albumin clearance (5 mg/kg body weight) with plasma bilirubin in jaundiced patients with and without cholangitis.* ●, *jaundiced without cholangitis;* ■, *cholangitis*

Blood endotoxin levels

Blood was taken from an antecubital fossa vein to measure systemic endotoxin levels in all patients before micro-aggregated albumin clearance studies. Plasma endotoxin levels were measured by a quantitative chromogenic limulus lysate method described previously[12]. Endotoxaemia was defined as plasma endotoxin levels above 100 pg/ml.

Statistical analysis

Correlation of reticulo-endothelial phagocytic function with plasma bilirubin, serum bile salt, transaminase, fibronectin, and systemic and portal endotoxin levels were performed with both Pearson's correlation and Spearman's ρ tests. Comparisons of unpaired data were performed using Student's t test.

Results

Reticulo-endothelial phagocytic function

Regression coefficients of the measured plasma half-life values of micro-aggregated albumin clearance were always $>0·985$. The mean (+s.e.m.) half-life clearance in the jaundiced patients was 16·8±0·5 min compared with 13·7±0·4 min in the 10 non-jaundiced controls. There was a highly significant difference between these two groups ($t=3·8$, d.f. = 33, $P<0·001$).

Relationship of liver function tests and phagocytic function

There was a highly statistically significant correlation (*Figure 1*) between phagocytic function and plasma bilirubin levels in jaundiced patients (Pearson's correlation 0·775, Spearman's ρ test 0·744, $P<0·001$), but not between phagocytic function and either serum bile salts, plasma transaminase (AST), fibronectin, or systemic plasma endotoxin levels.

Relationship of malignancy and phagocytic function

In the 16 jaundiced patients with malignant obstruction (mean plasma bilirubin 393 µmol/l) the mean micro-aggregated albumin clearance half-life was 17·3 min, while in those without a malignancy (mean bilirubin 200 µmol/l) the clearance was 15·9 min. As is shown in *Figure 2*, it is probably the depth of jaundice that results in a prolonged albumin clearance in those with a malignant obstruction rather than the malignancy *per se*.

Relationship of cholangitis and phagocytic function

The mean micro-aggregated albumin half-life clearance in the five jaundiced patients with cholangitis was 19·7 min, which was significantly prolonged compared with the other jaundiced patients ($t=2·39$, d.f. = 25, $P<0·05$). Furthermore, patients with cholangitis had prolonged albumin clearance in relation to their serum bilirubin levels (*Figure 1*).

Opsonin levels

The mean (±s.e.m.) fibronectin level in jaundiced patients was 324±21 µg/ml, and, although this was lower than in 25 non-jaundiced controls (mean 341±18 µg/ml), there was no significant difference between these groups ($t=0·6$, d.f. = 48, $P>0·5$). The mean (±s.e.m.) fibronectin level in jaundiced patients with cholangitis was 207±30 µg/ml which was significantly less than that of non-jaundiced control patients ($t=3·08$, d.f. = 28, $P<0·005$) and other jaundiced patients ($t=2·37$, d.f. = 28, $P<0·05$).

The mean (±s.e.m.) IgG in jaundiced patients was 9·6±0·5 g/l. All levels were within the normal range (5·4–17·2 g/l) except in two patients whose levels were slightly below normal. The five jaundiced patients with cholangitis had IgG levels within the normal range.

The plasma complement component levels of patients with obstructive jaundice were within normal limits for C3/C3c, βlH, and factor B, but were slightly raised for C4 (mea 134 per cent compared with pooled normal levels).

Opsonic activity

Opsonic phagocytic activities of sera from all jaundiced patient were greater than the pooled normal sera. Expressed as percentage of pooled normal sera the opsonic activity of th jaundiced sera ranged from 106 to 316 per cent.

Sinusoidal blood flow

There was no statistically significant difference in hepati sinusoidal blood flow between jaundiced and non-jaundice patients. The mean (±s.e.m.) clearance half-life for 0·5 m micro-aggregated albumin/kg body weight in ten jaundice patients was 5·1±0·3 min compared with 4·9±0·3 min in 1 non-jaundiced controls. Sinusoidal blood flow was no measured in patients with cholangitis.

Endotoxin levels

Only five jaundiced patients had endotoxaemia in the systemi blood at the time of the phagocytic test. The mean albumi clearance in these patients was 18·2 min compared with 16·4 mi in the remainder of the jaundiced patients. There was n statistically significant difference between these two groups.

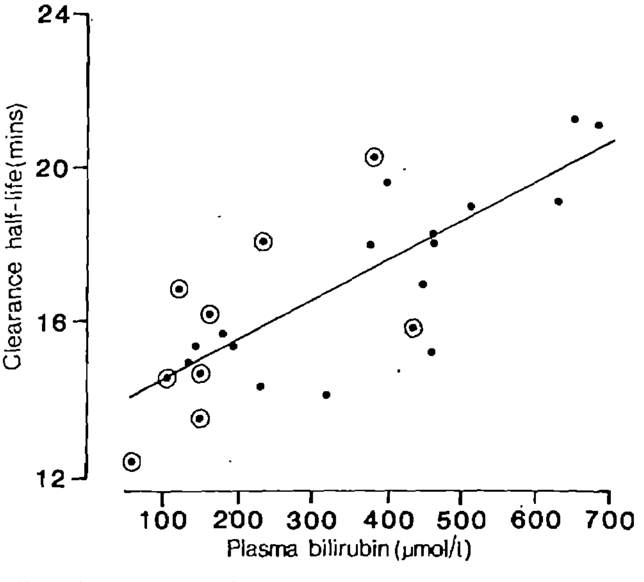

Figure 2 *Correlation of micro-aggregated albumin clearance (5 mg/k body weight) with plasma bilirubin in patients with malignant and non malignant obstructive jaundice.* ⊙, *non-malignant;* ●, *malignant*

Discussion

Reticulo-endothelial phagocytic function

Clearance of intravenous micro-aggregated albumin has been used frequently to measure reticulo-endothelial phagocytic function in man[4,13–16]. The organ distribution and plasma half-life of micro-aggregated albumin are similar to that of carbon particles[7] which are taken up by the Kupffer cells within the liver[17,18].

There was a statistically significant prolongation of albumin clearance in patients with obstructive jaundice compared with the non-jaundiced controls. There was a strong correlation between albumin clearance and the plasma bilirubin level. Kuratsune *et al.*[19] demonstrated a negative correlation between reticulo-endothelial phagocytic function and systemic endotoxaemia in patients with cirrhosis and concluded that endotoxaemia resulted from depressed phagocytic function allowing spillover of endotoxins from the portal circulation. A similar action may occur in obstructive jaundice. The relationship between bilirubin level and phagocytic function may partly account for the increased incidence of systemic endotoxaemia in deeply jaundiced patients. We have previously found that there is no significant difference between portal endotoxin levels in jaundiced patients with plasma bilirubin levels above or below 200 μmol/l. But whereas 55 per cent of patients with a bilirubin level above 200 μmol/l have systemic endotoxaemia, it is present in only 11 per cent of patients with a bilirubin level below[12] 200 μmol/l. In the present study only five jaundiced patients had systemic endotoxaemia at the time of the reticulo-endothelial studies, and although the albumin clearance was delayed in these patients compared with other jaundiced patients (18·2 *versus* 16·4 min) the numbers of patients are too small to allow any firm conclusions to be drawn.

No statistically significant correlation existed between phagocytic function and either bile salt or transaminase levels. Alterations to cell membranes, cellular function and Kupffer cell morphology have been attributed to the detergent properties of bile salts[20–26]. Nevertheless, reduced reticulo-endothelial phagocytic function is present in parenchymal liver diseases which are not associated with high blood bile salt levels[27,28].

Margarey and Baum[14] found that patients with a small primary malignancy had reduced phagocytic function, whereas those with a large primary or metastatic disease had increased function. In our study, patients with malignant obstruction had depressed function, but this was probably related to the higher plasma bilirubin levels in these patients (*Figure 2*).

In the five patients with cholangitis the albumin clearance was significantly prolonged compared to other jaundiced patients (*Figure 3*), and was associated with low fibronectin levels. The reduced reticulo-endothelial function and opsonin levels in these patients may contribute to endotoxaemia and the high incidence of renal failure that commonly occurs[29].

Opsonin levels and activity

Reticulo-endothelial depression following surgery, trauma, burns and haemorrhagic shock correlates closely with deficits in fibronectin levels[30–33]. Fibronectin levels have been reported to be raised[34] and lowered[35] in obstructive jaundice. These differences probably relate to the relatively few numbers of patients studied and possibly the different assays used. In the present study, mean plasma levels of fibronectin were normal in jaundiced patients without cholangitis, and there was a poor correlation between albumin clearance and fibronectin levels. Patients with cholangitis had a significant reduction in fibronectin levels, and this may have been due to an increased consumption in the presence of infection.

Mean levels of serum IgG were within normal limits in jaundiced patients, as has been found in previous studies[36,37]. Although Morrison *et al.*[38] found higher complement levels in patients with obstructive jaundice, in the present study, levels of the complement components C3/C3c, β1H and factor B were all normal. C4 levels were raised, but this may just reflect an acute phase protein response.

The opsonic activity of sera from jaundiced patients as measured by the opsonin mediated phagocytosis of yeast *in vitro* was increased. Enhanced yeast opsonization has also been found in children with biliary atresia[39]. Therefore no reduction in opsonin levels of activity that would account for defective reticulo-endothelial function in patients with obstructive jaundice has been demonstrated.

Hepatic sinusoidal blood flow

Alteration of hepatic sinusoidal perfusion is a potentially important determinant of reticulo-endothelial function. Depressed phagocytosis associated with a decreased hepatic sinusoidal perfusion occurs in patients with alcoholic cirrhosis[40]. No alteration in the hepatic sinusoidal blood flow occurs in bile duct ligated dogs[41] and, in the present study, blood flow was found to be normal in jaundiced patients.

Other factors

There are some other factors that may influence reticulo-endothelial function in obstructive jaundice that have not been investigated in this study. These include the effects of portal endotoxin levels, alteration in the morphology or numbers of Kupffer cells and the saturation of reticulo-endothelial cell membrane receptors.

It is unlikely that portal endotoxaemia produces depression of reticulo-endothelial function. Cultured Kupffer cells can be incubated *in vitro* with up to 3 mg/ml endotoxin for 5 h without loss of viability[42], and endotoxin rather than depresing the reticulo-endothelial system has been used as a means of inducing phagocytic activity[43,44].

A reduction in Kupffer cell numbers may lead to reduced reticulo-endothelial function. Rats with obstructive jaundice also have impaired micro-aggregated albumin clearance, and immunohistochemical studies show that there is a paradoxical increase in the number of Kupffer cells, but they do not appear to be activated[6,45]. No studies of Kupffer cell population in man have been reported.

The reticulo-endothelial system is responsible for the clearance of particulates from the blood, including immune complexes, aggregated platelets, fibrin and fibrinogen degradation products (FDP). Experimental defibrinogenation increases FDP and depresses phagocytic function[46] which is probably due to fibrin and FDP becoming attached to the surface of the reticulo-endothelial cells[47]. Raised levels of FDP can be detected in patients with obstructive jaundice and disseminated intravascular coagulation occasionally has been reported[48–51]. However, raised FDP levels are common in non-jaundiced patients awaiting surgery[52,53].

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References

1. Bailey ME. Endotoxin, bile salts and renal function in obstructive jaundice. *Br J Surg* 1976; 63: 774–8.
2. Pain JA, Cahill CJ, Bailey ME. Perioperative complications in obstructive jaundice: therapeutic considerations. *Br J Surg* 1985; 72: 942–5.
3. Bradfield JWB. Control of spillover: the importance of Kupffer cell function in clinical medicine. *Lancet* 1974; ii: 883–6.
4. Drivas G, James O, Wardle N. Study of reticuloendothelial phagocytic capacity in patients with cholestasis. *Br Med J* 1976; 1: 1568–9.

5. Biozzi G, Stiffel C. The pathophysiology of the reticuloendothelial cells of the liver and spleen. In: Popper H, ed. *Progress in Liver Disease*. New York: Grune, 1965: 166–91.
6. Pain JA, Collier DStJ, Ritson A. Reticuloendothelial system phagocytic function in obstructive jaundice and its modification by a muramyl dipeptide analogue. *Eur Surg Res* 1987; **19**: 16–22.
7. Benacerraf B, Biozzi G, Halpern BN, Stiffel C, Mouton D. Phagocytosis of heat denatured human serum albumin labelled with ^{131}I and its use as a means of investigating liver blood flow. *Br J Exp Pathol* 1957; **38**: 35–48.
8. Iio M, Wagner HN. Studies of the reticuloendothelial system (RES). I. Measurement of the phagocytic capacity of the RES in man and dog. *J Clin Invest* 1963; **42**: 417–26.
9. Mashige F, Imai K, Osuga T. A simple and sensitive assay of total serum bile acids. *Clin Chim Acta* 1976; **70**: 79–86.
10. Osuga T. Mitamura K, Mashige F, Imai K. Evaluation of fluorometrically estimated serum bile acid in liver disease. *Clin Chim Acta* 1977; **75**: 81–9.
11. Kerr MA, Falconer JS, Bashey A, Swanson Beck J. The effect of C3 levels on yeast opsonization by normal and pathological sera: identification of a complement independent opsonin. *Clin Exp Immunol* 1983; **54**: 793–800.
12. Pain JA, Bailey ME. Measurement of operative endotoxin levels in jaundiced and non-jaundiced patients. *Eur Surg Res* 1987; **19**: 207–16.
13. Sheagren JN, Block JB, Wolff SM. Reticuloendothelial system phagocytic function in patients with Hodgkin's disease. *J Clin Invest* 1967; **46**: 855–62.
14. Margarey CJ, Baum M. Reticulo-endothelial activity in humans with cancer. *Br J Surg* 1970; **57**: 748–52.
15. Schildt B, Gertz I, Wide L. Differentiated reticuloendothelial system (RES) function in some critical surgical conditions. *Acta Chir Scand* 1974; **140**: 611–17.
16. Palmer KR, Barber DC, Sherriff SB, Holdsworth CD. Reticuloendothelial function in coeliac disease and ulcerative colitis. *Gut* 1983; **24**: 384–8.
17. Zweifach BW, Benacerraf B, Thomas L. The relationships between the vascular manifestations of shock produced by endotoxin, trauma, and hemorrhage. II. The possible role of the reticuloendothelial system in resistance to each type of shock. *J Exp Med* 1957; **106**: 403–14.
18. Di Luzio NR. Influence of glucan on hepatic macrophage and function: relation to inhibition of hepatic metastases. In: Wisse E, Knook DL, eds. *Kupffer Cells and Other Liver Sinusoidal Cells*. Amsterdam: Elsevier/North Holland Biomedical Press, 1977: 397–406.
19. Kuratsune H, Koda T, Kurahori T. The relationship between endotoxin and the phagocytic activity of the reticuloendothelial system. *Hepato-gastroenterol* 1983; **30**: 79–82.
20. Hofmann AF, Small DM. Detergent properties of bile salts: correlation with physiological function. *Ann Rev Med* 1967; **18**: 333–76.
21. Schaffner F, Bacchin PG, Hutterer F *et al*. Mechanism of cholestasis. 4. Structural and biochemical changes in the liver and serum in rats after bile duct ligation. *Gastroenterology* 1971; **60**: 888–97.
22. Bertok L. Physico-chemical defense of vertebrate organisms: the role of bile acids in defense against bacterial endotoxins. *Perspect Biol Med* 1977; **21**: 70–6.
23. Vyvoda OS, Coleman R, Holdsworth G. Effects of different bile salts upon the composition and morphology of a liver plasma membrane preparation. *Biochim Biophys Acta* 1977; **465**: 68–76.
24. Holdsworth G, Coleman R. Plasma-membrane components can be removed from isolated lymphocytes by the bile salts glycocholate and taurocholate without cell lysis. *Biochem J* 1976; **158**: 493–5.
25. Popper H. Summary. In: Wisse E, Knook DL, eds. *Kupffer Cells and Other Liver Sinusoidal Cells*. Amsterdam: Elsevier/North Holland Biomedical Press, 1977: 509–14.
26. Keane RM, Gadacz TR, Munster AM, Birmingham W, Winchurch RA. Impairment of human lymphocytic function by bile salts. *Surgery* 1984; **95**: 439–43.
27. Liu YK. Phagocytic capacity of reticuloendothelial system in alcoholics. *J Reticuloendothelial Soc* 1979; **25**: 605–13.
28. Canalese J, Gove CD, Gimson AES, Wilkinson SP, Wardle EN, Williams R. Reticuloendothelial system and hepatocyte function in fulminant hepatic failure. *Gut* 1982; **23**: 265–9.
29. Bismuth H, Kuntziger H, Corlette MB. Cholangitis with acute renal failure. *Ann Surg* 1975; **181**: 881–7.
30. Saba TM. Effect of surgical trauma on the clearance and localization of blood-borne particulate matter. *Surgery* 1972; **71**: 675–85.
31. Saba TM. Reticuloendothelial systemic host defense after surgery and traumatic shock. *Circ Shock* 1975; **2**: 91–108.
32. Scovill WA, Saba TM, Kaplan JE, Bernard H. Deficits in reticuloendothelial humoral control mechanisms in patients after trauma. *J Trauma* 1976; **16**: 898–904.
33. Saba TM, Cho E. Reticuloendothelial (RE) response to surgery as modified by intravenous administration of plasma cryoprecipitate or cold-insoluble globulin (plasma fibronectin) purified by affinity chromatography. *Adv Shock Res* 1980; **3**: 251–71.
34. Stathakis NE, Fountas A, Tsianos E. Plasma fibronectin in normal subjects and in various disease states. *J Clin Pathol* 1981; **34**: 504–8.
35. Llena Puy MC, Cuestra Munoz J, Munoz Y, Fernandez JR, Tres Sanchez A. Fibronectina y colostasis hepatica. *Rev Clin Esp* 1984; **175**: 63–5.
36. LoGrippo GA, Anselm K, Hayashi H. Serum immunoglobulins and five serum proteins in extrahepatic obstructive jaundice and alcoholic cirrhosis. *Am J Gastroenterol* 1971; **56**: 357–63.
37. Fucikova T. Immunoglobulins in liver diseases. *Acta Univ Carol* 1974; **62**: 90–5.
38. Morrison L, Blamey S, Veitch J, Brown I, Whaley K. Complement levels in serum and bile in patients with extrahepatic biliary tract obstruction. *J Clin Lab Immunol* 1984; **13**: 71–4.
39. Larcher VF, Wyke RJ, Vergani D, Mowat AP, Williams R. Yeast opsonisation and complement in children with liver disease. Analysis of 69 cases. *Pediatr Res* 1983; **17**: 296–300.
40. Cooksley WGE, Powell LW, Halliday JW. Reticuloendothelial phagocytic function in human liver disease and its relationship to haemolysis. *Br J Haematol* 1973; **25**: 147–63.
41. Ohlson EG. The effect of biliary obstruction on the distribution of the hepatic blood flow and reticuloendothelial system in dogs. *Acta Chir Scand* 1972; **138**: 159–64.
42. Ramadori G, zum Buschenfelde KHM. Hepatic uptake of endotoxin. *Gastroenterology* 1982; **83**: 521–2.
43. Jenkin C, Palmer DL. Changes in the titre of serum opsonins and phagocytic properties of mouse macrophages following injection of endotoxin. *J Exp Med* 1960; **112**: 419–22.
44. Greisman SE, Carroza FA, Hills JD. Mechanisms of endotoxin tolerance. I. Relationship between tolerance and reticuloendothelial system phagocytic activity in the rabbit. *J Exp Med* 1963; **117**: 663–74.
45. Collier DStJ, Pain JA, Wight DGD, Lovat P, Bailey ME. The Kupffer cell in experimental extrahepatic cholestasis in the rat—a light microscopy, immunohistochemical and electron microscopy study. *J Pathol* 1986; **150**: 187–94.
46. Ahlgren T, Berghem L, Lahnborng G. Phagocytic and catabolic function of the reticuloendothelial system in dogs subjected to defibrinogenation. In: Wisse E, Knook DL, eds. *Kupffer Cells and Other Liver Sinusoidal Cells*. Amsterdam: Elsevier/North Holland Biomedical Press, 1977: 373–8.
47. Emeis JJ, Lindeman J. Rat liver macrophages will not phagocytose fibrin during disseminated intravascular coagulation. *Haemostasis* 1976; **5**: 193–210.
48. Jedrychowski A, Hillenbrand P, Ajduklewicz AB, Parbhoo SP, Sherlock S. Fibrinolysis in cholestatic jaundice. *Br Med J* 1973; **1**: 640–2.
49. Wardle EN. Fibrinogen in liver disease. *Arch Surg* 1974; **109**: 741–6.
50. Takeda S, Takaki A, Ohsato K. Occurrence of disseminated intravascular coagulation (DIC) in obstructive jaundice and its relation to biliary tract infection. *Jpn J Surg* 1977; **7**: 82–9.
51. Allison MEM, Prentice CRM, Kennedy AC, Blumgart LH. Renal function and other factors in obstructive jaundice. *Br J Surg* 1979; **66**: 392–7.
52. Hunt DR, Allison MEM, Prentice CRM, Blumgart LH. Endotoxaemia, disturbance of coagulation and obstructive jaundice. *Am J Surg* 1982; **144**: 325–9.
53. Ingoldby CJ, McPherson GAD, Blumgart LH. Endotoxemia in human obstructive jaundice. Effect of polymixin B. *Am J Surg* 1984; **147**: 766–71.

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Morbidity and mortality of common bile duct exploration

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This retrospective study reviews the complications which occurred in 257 patients who had supraduodenal exploration of the common bile duct in one hospital during a 15-year period. One hundred and eighteen patients (46 per cent) developed complications: septic and cardiorespiratory complications were most common, occurring in 19·5 per cent and 16·7 per cent of patients respectively. Postoperative retained stones were detected in 37 patients (14 per cent), causing complications in 54 per cent. Peroperative postexploratory cholangiography did not significantly reduce the incidence of this problem. None of the 12 patients who had postexploratory choledochoscopy had retained stones. Five patients (1·9 per cent) died, three of whom had duct procedures in addition to supraduodenal exploration and two of whom had retained stones. It is concluded that common bile duct exploration has a high associated morbidity, particularly due to sepsis and retained stones.

Keywords: Common bile duct exploration, complications

Cholecystectomy is one of the most commonly performed procedures in UK surgical practice today. In 13–26 per cent of cases[1–8] it is accompanied by exploration of the common bile duct (CBD), using the supraduodenal (SD) or transduodenal (TD) approach or occasionally a combination (SD+TD) of both. As most surgeons use the supraduodenal route, it is surprising to find that little information exists on the morbidity and mortality associated with this procedure in UK surgical practice. We have therefore undertaken a 15-year retrospective study to assess the complications of this procedure, for operations carried out by consultants and registrars in a district general hospital.

Patients and methods

The operating theatre register was used to identify 311 patients who had undergone CBD exploration by the supraduodenal route at the East Glamorgan General Hospital over a 15-year period from 1969 to 1984. A total of 257 of these patients' case notes were reviewed, the remainder being excluded either because of the finding of a malignancy at operation (21) or because comprehensive case notes were not available (33). The patients, whose ages ranged from 26 to 85 years (mean age 57·4 years), were under the care of three surgical firms and operations were carried out by registrars ($n=60$) or consultant surgeons ($n=197$). The majority of patients (65 per cent) were women, the sex difference being most marked in the younger age groups (*Figure 1*); only 12 of the 73 patients (16·4 per cent) under the age of 50 years were male ($P<0·001$).

All patients had common bile duct exploration carried out initially by the supraduodenal route, but 39 had additional transduodenal exploration and 9 had a postexploration choledochoduodenostomy. Twenty-eight of the patients had had at least one previous operation on their biliary tree carried out between 1 week and 40 years previously: this constituted cholecystectomy alone (15 patients), common bile duct exploration with or without cholecystectomy (12 patients) or choledochoduodenostomy (1 patient).

A data sheet consisting of 73 variables was completed for each hospital admission and included clinical, radiological, haematological, biochemical and operative details. When recording pre-operative laboratory and radiological investigations, the most recent results before operation were always taken. In assessing morbidity, details of all complications, irrespective of whether or not they were causing symptoms, were recorded. Out-patient follow-up notes were also scrutinized. These were available for up to 15 years after discharge in some patients with a mean follow-up duration of 34 months.

Complications were divided into operative and non-operative, depending on whether or not they were a direct result of the surgical procedure. Septic complications include all postoperative infective complications regardless of whether they were directly attributable to biliary disease or to the surgical procedure *per se*. In wound infections, where possible, the organism responsible was noted, as were organisms cultured peroperatively from the bile. A diagnosis of septicaemia was accepted only when a confirmatory positive blood culture report was available. Postoperative peritonitis was divided into generalized or localized (abscess) and was diagnosed either operatively, or at autopsy examination, or, in the case of two abscesses, by ultrasound examination alone. A diagnosis of ascending cholangitis was accepted on clinical grounds provided that there was recorded evidence of an intermittent spiking pyrexia. Extravasation of bile from the wound or a drain site at any stage, or from the T-tube site for more than 5 days after its removal, was recorded as a biliary fistula. Chest infections were diagnosed as present on the basis of either clinical or radiological signs alone, although the frequent radiological finding of transient right basal atelectasis on the first postoperative day was disregarded.

The result of the postoperative T-tube cholangiogram was used in calculating the immediate retained stone rate. However, in an attempt to evaluate the overall incidence of this problem, retained stones discovered after discharge of the patient from hospital were also recorded. In order to exclude, as far as possible, primary recurrent stones, late retained stones were defined as stones found in patients within 1 year of the primary operation[9], or those found in patients who had recurrent symptoms from the time of operation or stones identified within 5 years of operation in a normal calibre biliary tree.

Postoperative mortality was defined as death within 30 days of operation or during the index hospital admission. Autopsy details were available on all but one of the patients who died. To ensure accuracy in

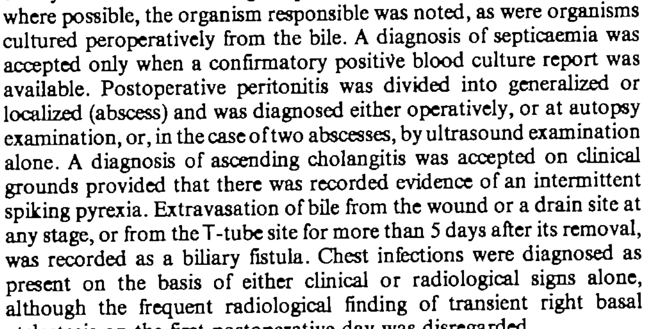

Figure 1 *Distribution of patients by age and sex.* □, *male;* ▧, *female*

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Table 1 *Summary of complications of common bile duct exploration* (n=*118*)

	n	Percentage
Procedure-related		
Sepsis	50	19·5
Retained stones	37	14
Wound dehiscence/incisional hernia	10	3·9
T-tube complications	9	3·5
Pancreatitis	5	1·9
Prolonged ileus	5	1·9
Biliary fistula	4	1·6
Bleeding	3	1·2
General		
Cardiorespiratory	43	16·7
Urinary tract	6	2·3
Bleeding	3	1·2
Renal failure	3	1·2
Hepatic failure	1	0·4
Psychosis	1	0·4

Table 2 *Septic complications in 50 patients*

	n	Percentage
Wound infection	41	15·9
Peritonitis		
Localized	6	2·3
Generalized	3	1·2
Ascending cholangitis	5	1·9
Septicaemia	3	1·2

calculating the mortality rate, ward nursing notes were reviewed in those patients whose case notes were not available.

Statistical analysis was carried out using the Unistat (Unisoft Ltd) statistical package. In assessing the association between different variables and subsequent complications, only those factors were analysed where the presence or absence of the variable was recorded in the notes in at least 70 per cent of cases. Significance values, where quoted refer to χ^2 or Fisher's exact tests.

Results

A total of 118 patients (46 per cent) developed one or more complications, including asymptomatic retained stones (*Table 1*). If one disregards retained stones discovered after discharge of the patient from hospital[7,10–13], then the complication rate decreases to 41 per cent. Patients with complications had a mean hospital stay of 18·9 days, compared within 13·1 days in those without complications (overall mean stay 15·6 days).

Sepsis accounted for the largest group of complications (*Table 1*), with wound infections predominating (*Table 2*). Organisms were isolated from the wounds of 39 of the 41 patients with wound infections (there was no record of material being sent for culture in 2 patients with purulent wound discharges). Specimens of bile had been taken for culture during operation in 35 of the patients with wound infections and in 28 of these patients (80 per cent) the same organisms were isolated from the infected wound postoperatively. Gram-negative intestinal organisms were the most common isolates from wounds, with *Escherichia coli* being found in 49 per cent of cases. Prophylactic antibiotics which, it should be noted, were not in routine use during the early years of this study, were given to 102 patients (40 per cent). Their use was associated with a decrease in wound infection rate (from 20 per cent to 12 per cent) and the overall septic complication rate (from 23·9 per cent to 16·7 per cent).

Of the many different variables analysed, only pre-existing unrelated disease was associated with significantly increased postoperative morbidity. Such disease was present in 105 patients and was associated with a complication rate of 49 per cent as opposed to 32 per cent in otherwise healthy patients ($P<0{\cdot}01$). This increased morbidity was mainly due to cardiorespiratory complications, which were almost twice as common (23 per cent *versus* 12 per cent, $P<0{\cdot}05$, χ^2 test). Increased complication rates which did not reach statistical significance were associated with a number of other factors including emergency hospital admission, age greater than 65 years, pre-operative leucocytosis and cigarette smoking. Previous surgery to the biliary tree, mode of duct closure (primary closure or T-tube insertion) and jaundice on admission did not appear to have any influence on the complication rate. Operation by a non-consultant surgeon was not associated with significantly different overall complication rates (40 per cent) or retained stone rates (18 per cent) when compared with operations carried out by a consultant surgeon (48 per cent and 14 per cent respectively).

In 236 patients T tubes were left *in situ* after CBD exploration. Nine of these patients (4 per cent) developed complications directly attributable to the T tube or to the postoperative T-tube cholangiogram. Intraperitoneal leakage of contrast medium was seen in five patients, three of whom subsequently developed peritoneal sepsis (generalized peritonitis in two and a subhepatic abscess in one patient). Septicaemia occurred in two patients at the time of postoperative T-tube cholangiogram and two other patients developed prolonged bile leaks from the T-tube site after tube removal. Biliary fistulae occurred in two other patients: one from a peritoneal drain site and one from the operation wound.

The most common non-operative complications were cardiorespiratory in origin, with chest infections predominating (11·3 per cent). Three patients developed upper gastrointestinal bleeding postoperatively from causes unrelated to the operative procedure on the biliary tree. There was one case of hepatorenal failure, occurring in a patient who was jaundiced at the time of operation.

Peroperative pre-exploratory cholangiography was performed in 200 patients (78 per cent), usually via a cannula placed in the cystic duct or a needle inserted into the common bile duct. Despite this, the negative exploration rate in this study was 22·3 per cent although three of these patients were subsequently found to have retained stones postoperatively. Complications occurred in 39·3 per cent of the patients who had had a negative exploration and included two deaths (3·6 per cent), one of which may have been directly related to the exploration.

A total of 37 patients (14 per cent) had retained stones. These were discovered before discharge from hospital in 20 patients (8 per cent), and in the remainder at intervals varying from 1 week to 5 years. Postexploratory (completion) cholangiography to confirm clearance of the ducts was usually performed by injection of dye through the T tube, and was carried out in 103 patients (40 per cent). Its use did not significantly decrease the rate of retained stones (*Table 3*). The 22 patients who had repeat exploration of the common bile duct during the original operation on the basis of an 'abnormal' postexploratory cholangiogram as interpreted by the operating surgeon had a

Table 3 *The value of postexploratory cholangiography in prevention of retained stones*

		Retained stones	
Cholangiography	*n*	*n*	Percentage
Performed	103	14	13·6*
Not performed	124	22	17·7*
Not recorded	30	1	

* Not significant

retained stone rate of 31·8 per cent. This was significantly higher ($P<0·02$, χ^2 test) than the rate (18·6 per cent) in the 81 patients where the surgeon interpreted the cholangiogram as normal. Although in only 12 patients was peroperative choledochoscopy carried out, none of these patients subsequently had retained stones. Retained stones eventually caused complications in 20 patients (54 per cent) including biliary colic/jaundice in 14 (38 per cent), pancreatitis in 3 (8 per cent) and ascending cholangitis in 3 (8 per cent). The modes of management of retained stones are shown in *Table 4*.

Table 4 *Mode of management of retained stones in 37 patients*

Management	*n*
Surgical removal	11
'Radiological' removal	3
Patient died	2
Passed spontaneously	1
No intervention	20

Table 5 *Mortality details in five patients (time of death is given in days after surgery)*

Sex	Age (years)	Procedure*	Day	Details
F	62	SD	10	Myocardial infarction
F	67	SD+CDD	7	Bile peritonitis after surgery
M	72	SD+TD	3	Postop. acute haemorrhagic pancreatitis, renal failure, residual stones
M	76	SD+TD	46	Jaundice on admission. Postop. acute pancreatitis, subphrenic abscess, hepatic failure, residual stones
M	87	SD	19	Ascending cholangitis pre-op. Postop. septicaemia

* SD, supraduodenal exploration; TD, transduodenal exploration; CDD, choledochoduodenostomy

The mortality rate for supraduodenal exploration in this series was 1·9 per cent. This compares with a mortality rate of just under 0·6 per cent in the 1705 patients undergoing cholecystectomy alone during the same period. Details of the five patients who died are given in *Table 5*. Three of these patients had further procedures carried out in addition to supraduodenal duct exploration, including two who also had a transduodenal approach. The latter approach carried a 5 per cent mortality rate in this series, whereas exploration by the supraduodenal route alone was associated with a mortality of only 1 per cent. Patient age greater than 65 years was associated with a 4·1 per cent mortality risk, in comparison with a 0·6 per cent risk in younger patients ($P<0·05$). Similarly, the presence of clinical jaundice on admission was associated with a higher mortality rate (4·6 per cent) than that encountered in non-icteric patients ($P<0·05$).

Discussion

This study is a complete review of 257 patients who had undergone common bile duct exploration in a district general hospital. Although retrospective, it is a useful reflection of the true morbidity and mortality of this procedure in the UK, and allows comparison with the results of endoscopic sphincterotomy. To our knowledge, this study also represents the largest UK series available to date (*Table 6*).

The overall morbidity rate of 46 per cent is similar to that reported in other series, where the supraduodenal approach has been the principal method of exploration[7,16]. Unlike other authors, morbidity assessment has included retained stones found in patients who did not develop any other complications, because of their serious potential morbidity. The negative exploration rate is also comparable to that of other series (*Table 6*). Operator experience *per se* did not significantly affect the overall morbidity rate. However, the frequency with which individual surgeons carry out CBD exploration must be relatively low, as the rate of exploration in this series was only 6·9 cases per surgical firm annually. This rate is somewhat lower

Table 6 *UK series providing morbidity/mortality data on common bile duct exploration (1965–85)*

					Rates (percentage)			
Reference	Centre	Year	Procedure*	*n*	Morbidity	Mortality	Retained stones	Negative exploration
7	Wrexham	1985	SD	57	44	1·8	—	—
			SD+CDD	57	42	3·3	—	—
			SD+TD	40	55		—	—
14	Edinburgh	1985	SD	166	—	—	—	—
			SD+TD	32	—	—	—	—
8	Stirling	1985	TD	54	—	3·7	1·9	—
3	York	1984	TD	118	—	2·5	0	14·5
4	Chester	1984	TD	174	—	10·3	—	—
			SD+TD	40	—	12·5	—	—
5	Southampton	1984	SD	103	—	0	5·8	—
6	Hammersmith	1984	most SD	62	—	1·6	5·3	28
2	Mansfield	1982	?	153	—	4·6	—	29
12	Belfast	1980	most SD	94	—	3·5	11·2	40
1	Cheltenham	1979	SD	78	—	2·5	7·7	—
			TD	32	—	9·6	0	—
			TD+SD	12	—	33	8·3	—
15	Cardiff	1978	SD+TD	42	19	0	0	—

* SD, Supraduodenal exploration; TD, transduodenal exploration; CDD, choledochoduodenostomy

than that calculated from other series[1,3–5,7,8,12] in which the rate varies from 8 to 14·7 cases per firm annually.

Although this study was specifically undertaken to assess the complications of supraduodenal exploration for stones, a number of patients had additional procedures carried out on their biliary tree. These included an additional transduodenal approach in 39 patients and choledochoduodenostomy in 9 patients. In common with other comparable series[4,7,17], where mortality rates of up to 12·5 per cent have been reported, the use of the combined approach was associated with a higher mortality rate. However, Aubrey achieved better results using the combined approach in a small series of selected patients[15]. Although the transduodenal route alone is preferred by some surgeons[3,8], the results of this approach in the UK are not encouraging, with one large study reporting a mortality rate of 10·3 per cent[4].

Duct closure without T-tube drainage (primary duct closure) was associated with a higher complication rate (58 per cent) in this series than closure using a T tube (45 per cent), but was carried out in only 12 patients. Most other studies report better results with primary duct closure[18–21] and some of the possible reasons for this have been identified by Keighley[18]. He related the high incidence of infective complications directly to infected T-tube bile and also noted a higher incidence of pancreatitis and thrombo-embolism in association with T-tube drainage. It has been suggested that the routine use of choledochoduodenostomy in preference to T-tube drainage reduces the risk of infective complications in patients with a common bile duct of diameter $>1{\cdot}5$ cm[22–24].

Postoperative septic complications, occurring in 19·5 per cent of this series, remain a major problem in patients undergoing CBD exploration, and wound infection rates of up to 26 per cent are reported[1,4,7,12,14,16–18]. The high septic complication rate may be related to the widespread use of T tubes because of reasons discussed earlier. The reduction in the rate of septic complications by antibiotic prophylaxis was not as striking in this study as in others[18]. This may be related to the fact that there was no specific antibiotic policy in use during the early period of this study and, with the benefit of hindsight, some of the antibiotics used might now be deemed inappropriate for prophylactic use in biliary surgery. Theoretical support for antibiotic prophylaxis is provided by the correlation between organisms cultured from infected wounds and those cultured from peroperative bile samples in this and other series[14,25]. Further support is provided by the strong association between common duct stones and the presence of infected bile (43–58 per cent of cases)[14,23,25]. High risk factors which indicate the need for antibiotic prophylaxis have been identified[26] and the use of selective antibiotic prophylaxis can reduce the risk of infective complications[27]. Our results support the use of routine antibiotic prophylaxis.

Postoperative pancreatitis, confirmed by serum amylase estimation, occurred in five patients (1·9 per cent), an incidence lower than that in other reports. However, it should be mentioned that routine serum amylase estimations were not carried out postoperatively in all patients. Where this has been done, up to 39 per cent of patients have biochemical evidence of pancreatitis[28], and an even higher incidence, up to 100 per cent, has been reported after transduodenal exploration[1,3,8,18,28]. Of the five patients with postoperative pancreatitis in this study, two died, both having had CBD exploration by the combined approach. The reported mortality rate from postoperative clinical pancreatitis is as high as 55 per cent[4].

The incidence of retained stones is greater than that reported in a number of other series from the UK (*Table 6*) and elsewhere[29–31], with rates varying from 2·6 per cent to 13·6 per cent for supraduodenal exploration. However, it should be noted that most authors base their retained stone rate on those found at the time of postoperative T-tube cholangiography, which, as our results show, may underestimate the magnitude of this problem by as much as one-half. The true retained stone rate may be even higher as some retained stones may have been excluded by the criteria used to identify primary recurrent stones. More than half the patients with retained stones developed serious complications, which in two patients were responsible for their eventual demise.

The use of completion cholangiography did not significantly reduce the incidence of retained stones in this study. Although its accuracy remains questionable[12,13,29,32], this investigation together with various techniques of instrumentation of the duc is still, for many surgeons, the principal method of confirming duct clearance during operation. For this reason, the appearance of the completion cholangiogram, as interpreted by the surgeon at the time of operation, was also evaluated and related to the subsequent incidence of postoperative retained stones. Despite what one might expect to be a more carefu repeat exploration of the biliary tree on the basis of the 'abnormal' completion cholangiogram, stones were overlooked in almost one-third of patients. In this series, completion cholangiography was performed using the T tube, and we accep that better visualization has been reported by injecting dye through a Foley catheter inserted first proximally and then distally into the biliary tree[33].

Our findings suggest that other means of confirmation o duct clearance peroperatively are required. Choledochoscopy was introduced only late in this study and its encouraging results are supported by other reports that it may offer the bes prospect of reducing the retained stone rate[5,6,11,34,35]. Given the high overall incidence of retained stones in this and othe series, we feel that choledochoscopy should be carried ou routinely following common bile duct exploration.

The mortality rate in this series is similar to that in others which review supraduodenal common bile duct exploration (*Table 6*). Similarly, higher death rates have been found in patients having additional transduodenal exploration[1,4,7,17] and we feel that this should not be carried out as a routine procedure. Others have also noted higher mortality rates among elderly patients[7,36].

In conclusion, supraduodenal CBD exploration has a significant morbidity, particularly due to sepsis and retained stones. The incidence of septic complications should be reduced by appropriate antibiotic prophylaxis. The best prospect o reducing the unacceptably high incidence of retained stones seen in this and other series, might be to place less reliance on postexploratory cholangiography and to carry out routine postexploratory choledochoscopy. The combined supraduodenal and transduodenal approach has a high associated mortality and should be avoided where possible.

References

1. Vellacott KD, Powell PH. Exploration of the common bile duct: a comparative study. *Br J Surg* 1979; **66**: 389–91.
2. Doyle PJ, Ward-McQuaid JN, McEwen-Smith A. The value o routine per-operative cholangiography—a report of 4000 cholecystectomies. *Br J Surg* 1982; **69**: 617–19.
3. Antrum RM, Hall R. Transduodenal sphincteroplasty: an analysis of 118 consecutive cases. *Br J Surg* 1984; **71**: 446–8.
4. Cave-Bigley DJ, Aukland P, Kane JF, Hardy EG. Transduodenal exploration of the common bile duct in a district general hospital. *Ann R Coll Surg Engl* 1984; **66**: 187–9.
5. Gartell PC, McGinn FP. Choledochoscopy: are stones missed? A controlled study. *Br J Surg* 1984; **71**: 767–9.
6. Stubbs RS, Blumgart LH. Exploration of the common bile duct. Effect of a change in policy in one surgical unit. *J R Coll Surg Edinb* 1984; **29**: 76–9.
7. Crumplin MKH, Jenkinson LR, Kassab JY, Whitaker CM, Al-Boutiaki FH. Management of gallstones in a district general hospital. *Br J Surg* 1985; **72**: 428–32.
8. Ramsay G, Hehir M, McNeill AD. Routine transduodenal sphincterotomy for common bile duct exploration. *J R Coll Surg Edinb* 1985; **30**: 348–52.
9. Glenn F. Postcholecystectomy choledocholithiasis. *Surg Gynecol Obstet* 1972; **134**: 249–52.
10. Way LW, Amirand WH, Dunphy JE. Management of choledocholithiasis. *Ann Surg* 1972; **176**: 347–57.

11. Finnis D, Rowntree T. Choledochoscopy in exploration of the common bile duct. *Br J Surg* 1977; **64**: 661–4.
12. Cranley B, Logan H. Exploration of the common bile duct—the relevance of the clinical picture and the importance of peroperative cholangiography. *Br J Surg* 1980; **67**: 869–72.
13. Rogers AL, Farma GJ, Beamer RL, Chang FC. Incidence and associated mortality of retained common bile duct stones. *Am J Surg* 1985; **150**: 690–3.
14. Armstrong CP, Dixon JM, Duffy SW, Elton RA, Taylor TV, Davis GC. Choledochotomy and sepsis in benign biliary disease. *J R Coll Surg Edinb* 1985; **30**: 343–7.
15. Aubrey DA, Edwards JL. The selective use of combined supraduodenal and transduodenal exploration of the common bile duct. *Br J Surg* 1978; **65**: 246–51.
16. Jarhult J. Biliary stone surgery. Results of exploration of the common bile duct in a small district general hospital. *Acta Chir Scand* 1981; **147**: 147–50.
17. Peel ALG, Bourke JB, Hermon-Taylor J, MacLean ADW, Mann CV, Ritchie HD. How should the common bile duct be explored? *Ann R Coll Surg Engl* 1975; **56**: 124–34.
18. Keighley MRB, Burdon DW, Baddeley RM, Dorricott NJ, Oates GD, Watts GT, Alexander-Williams J. Complications of supraduodenal choledochotomy: a comparison of three methods of management. *Br J Surg* 1976; **63**: 754–8.
19. Collins PG, Redwood CRM, Wynne-Jones G. Common bile duct suture without intraductal drainage following cholecystectomy. *Br J Surg* 1960; **47**: 661–7.
20. Collins PG. Further experience with common bile duct closure without intraductal drainage following choledochotomy. *Br J Surg* 1967; **54**: 854–6.
21. Chande S, Devitt JE. T tubes, the surgical amulet after choledochotomy. *Surg Gynecol Obstet* 1973; **136**: 100–2.
22. Lygidakis NJ. Choledochoduodenostomy in calculous biliary tract disease. *Br J Surg* 1981; **68**: 762–65.
23. Lygidakis NJ. Infective complications after choledochotomy. *J R Coll Surg Edinb* 1982; **27**: 233–7.
24. Lygidakis NJ. The incidence and significance of common bile duct dilatation in biliary calculous diseases. *World J Surg* 1984; **8**: 327–34.
25. Keighley MRB, Graham NG. Infective complications of choledochotomy with drainage. *Br J Surg* 1971; **58**: 764–8.
26. Keighley MRB, Flinn R, Alexander-Williams J. Multivariate analysis of clinical and operative findings associated with biliary sepsis. *Br J Surg* 1976; **63**: 528–31.
27. Gunn AA. Antibiotics in biliary surgery. *Br J Surg* 1976; **63**: 627–30.
28. Keighley MRB, Graham NG. The aetiology and prevention of pancreatitis following biliary tract operations. *Br J Surg* 1973; **60**: 149–52.
29. Hall RC, Sakiyalak P, Kim SK, Rogers LS, Webb WR. Failure of operative cholangiography to prevent retained common bile duct stones. *Am J Surg* 1973; **125**: 51–63.
30. Glenn F. Retained calculi within the biliary ductal system. *Ann Surg* 1974; **179**: 528–39.
31. Hauer-Jensen M, Karesen R, Nygaard K, Solheim K, Amlie E, Havig O, Vidal KO. Predictive ability of choledocholithiasis indicators. *Ann Surg* 1985; **202**: 64–8.
32. Corlette JB, Schatzki S, Ackroyd F. Operative cholangiography and overlooked stones. *Arch Surg* 1978; **113**: 729–34.
33. Myat Thu Ya, Robinson D, Gunn AA. Peroperative cholangiography. *Br J Surg* 1973; **60**: 711–12.
34. Kappas A, Alexander-Williams J, Keighley MRB, Watts GT. Operative choledochoscopy. *Br J Surg* 1979; **66**: 177–9.
35. Ernst D, Windsor CWO. The use of a rigid choledochoscope in exploration of the common bile duct. *Br J Surg* 1982; **69**: 463–4.
36. Houghton PWJ, Jenkinson LR, Donaldson LA. Cholecystectomy in the elderly: a prospective study. *Br J Surg* 1985; **72**: 220–2.

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Surgical management of strictures of the major bile ducts in recurrent pyogenic cholangitis

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Definitive surgical procedures were performed on 46 patients with strictures of the major bile ducts: dilatation of strictures was undertaken in 6 patients, hepatotomy and plastic repair in 2, biliary-enteric anastomosis in 18, and liver resection with or without drainage for the rest of the biliary tree in 20 patients. The overall operative morbidity was 21·7 per cent. Two patients died within 30 days of operation. One patient died of septicaemia after emergency dilatation of stricture while another died of sepsis from a leakage after hepatotomy and plastic repair. The median follow-up for the 44 patients who survived the operation was 43 months. All strictures reformed after dilatation within 2 months. Acute cholangitis occurred in six patients, two after dilatation of strictures (with documented recurrent stone formation in one), two after biliary-enteric anastomosis and two after liver resection. Thus, good clinical results were obtained in 38 out of 44 patients (86·4 per cent).

Keywords: Bile duct stricture, surgical management

Recurrent pyogenic cholangitis is a distinct clinical entity characterized by repeated attacks of bacterial infection of the biliary tree[1]. The extrahepatic and intrahepatic ducts may show dilatation and stricture, and they may contain calculi, debris (mainly bile pigments, epithelial cells, and mixed exudates), and sometimes frank pus[2,3]. The majority of patients with acute cholangitis respond to conservative treatment with antibiotics and intravenous fluid. Emergency operations to decompress the obstructed biliary systems are required when conservative treatment fails or in patients with septicaemia[1,2]. Unless conditions are favourable, definitive surgery to prevent future fatal recurrence is best left to subsequent elective operation[2,3].

The choice of definitive procedure is determined by the location of stones, location of the biliary strictures and the general condition of the patients. Strictures in subsegmental and peripheral ducts are difficult to correct. Fortunately, obstruction of these minor ducts does not produce jaundice and, even if cholangitis occurs, the mild symptoms may pass unnoticed and the infection is frequently resisted[4]. On the other hand, strictures in major bile ducts (common bile duct and its primary and secondary branches) can lead to unrelenting cholangitis, recurrent stone formation, liver abscesses, septicaemia and death[4,5]. As non-iatrogenic inflammatory strictures of the major bile ducts are uncommon, and treatment often gives unsatisfactory results[1,6], we review our experience of this condition.

Patients and methods

From 1979 to 1986, 46 patients with strictures of the major bile ducts have been treated by definitive procedures. All patients received gentamicin 2 mg/kg and cefazolin 2 g intravenously just before emergency operations or cefamandole 2 g intravenously before elective operations. There were 24 men and 22 women. Their ages ranged from 17 to 86 years (mean ± s.d. was 55·8 ± 12·6 years). The sites of the strictures are shown in *Figure 1*. Multiple strictures occurred in three patients (*Figure 2*).

Most patients had a long history of repeated cholangitis (*Figure 3*) and 82·6 per cent of patients had previous biliary tract surgery. The clinical presentations that led to the definitive procedures were repeated cholangitis responsive to conservative treatment in 24 patients (52·2 per cent), upper abdominal pain with deranged liver function tests in 11 patients (23·9 per cent), cholangitis with septicaemic shock in 8 patients (17·4 per cent) and cholangitis with pyogenic liver abscesses in 3 patients (6·5 per cent). The last 11 patients required emergency operations to decompress the obstructed biliary systems and drain pus. One patient died after emergency operation.

For the 45 patients undergoing elective definitive procedures, the strictures were demonstrated by T-tube cholangiography in 10 patients, endoscopic retrograde cholangiopancreatogram (ERCP) in 29 patients and percutaneous transhepatic cholangiogram (PTC) in 4 patients. Two patients required both ERCP and selective left PTC to demonstrate the full extent of the strictures.

Dilatation of strictures with balloon catheters was performed through the T-tube tracts in three patients who refused further open surgery. In two patients who had previously undergone ten and seven biliary operations respectively, further biliary operation was considered too dangerous and dilatation was done through a percutaneous transhepatic route created by an interventional radiologist. Stones proximal to the strictures were removed by this route. In the early part of this series, plastic repair with Y-V plasty was performed via a

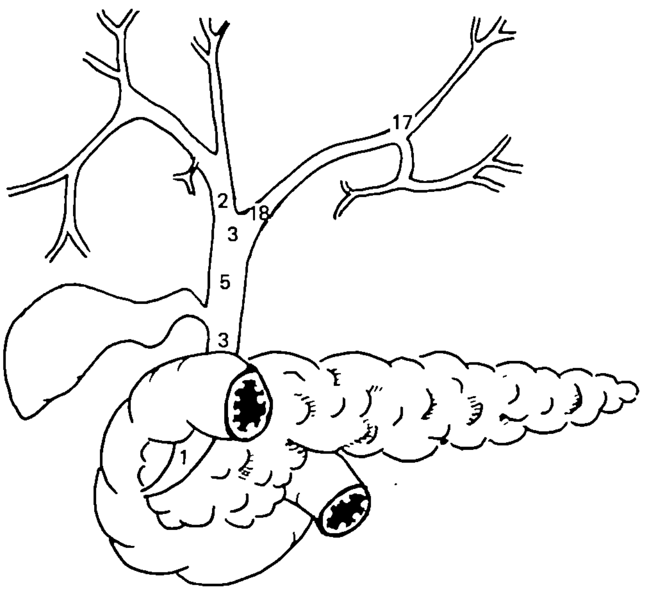

Figure 1 *Sites of strictures of major bile ducts in 46 patients (3 had multiple strictures)*

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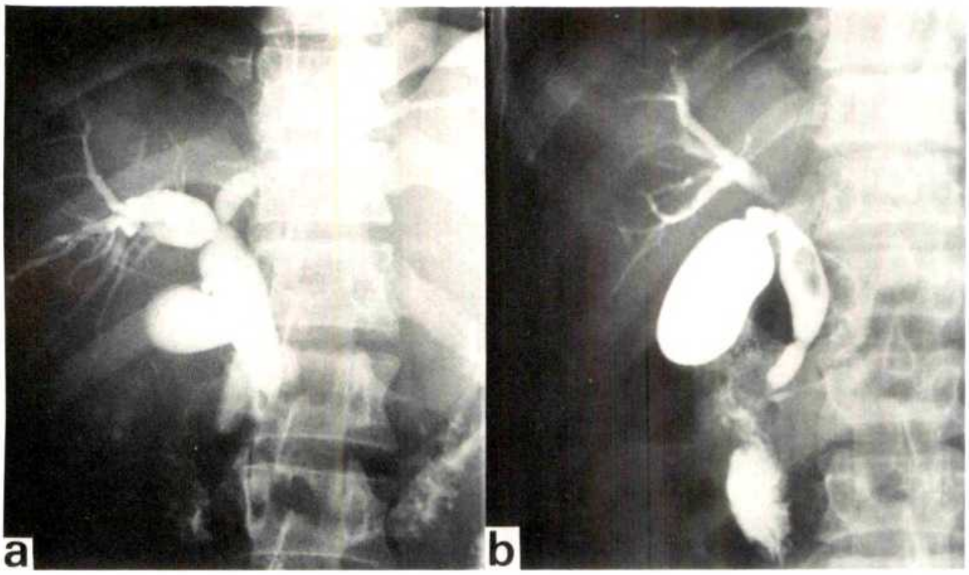

Figure 2 *Multiple strictures of major bile duct.* **a** *Strictures at origin of right and left hepatic ducts;* **b** strictures at common bile duct and common hepatic duct

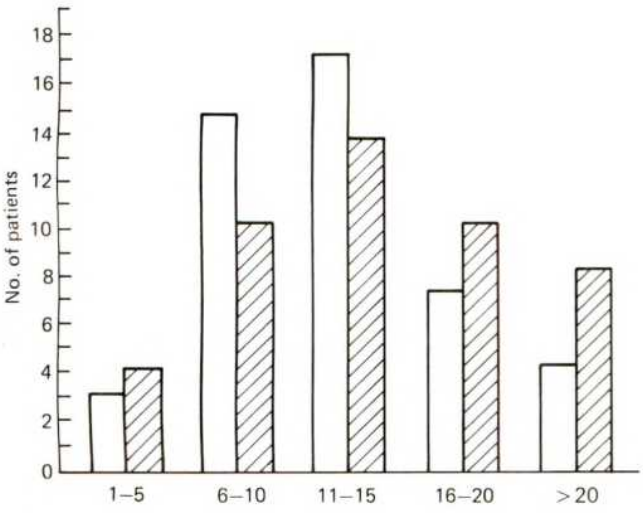

Figure 3 *Duration of symptoms and number of cholangitic attacks in patients with strictures of the major bile ducts.* □, *Number of attacks;* ▨, *duration of symptoms in years*

hepatotomy in two patients. Because of technical difficulty and failure in one patient this procedure has since been abandoned. For seven patients with strictures at the origin of the left duct and a relatively healthy left lobe of liver, a side to side left hepaticojejunostomy (Roux-en-Y) was carried out through the left duct approach[7]. Drainage procedures for the rest of the biliary system had either been performed previously or was carried out at the same operations in these seven patients. In 11 patients, the strictures were extrahepatic and drainage was achieved by choledochojejunostomy (3 patients), common hepaticojejunostomy (4 patients), or bilateral hepaticojejunostomy (4 patients). Hepatic resection was performed in 20 patients with atrophic liver segments proximal to the strictures. Resection combined with drainage procedures for the rest of the biliary tree was performed either at previous operation (nine patients) or at the same operation (seven patients). These drainage procedures included sphincteroplasty in nine patients, choledochojejunostomy in five patients and endoscopic papillotomy in two patients.

All stones in the biliary tree were removed with forceps, Dormia baskets, Fogarty catheters or saline flushing. Removal of stones from intrahepatic ducts and ducts proximal to strictures was facilitated by the use of flexible choledochoscopes (Fujinon CHO-S).

Results

Postoperative morbidity and mortality

There were no complications arising from dilatation except in one patient who died of septicaemia after emergency exploration of the common bile duct and dilatation of a left duct stricture. Of the 40 patients with open surgery, one with plastic repair developed leakage and a biliary fistula. He died of sepsis 2 months after surgery. There were five patients with postoperative chest infection, three with wound sepsis, one with a burst abdominal wound and one with a subphrenic abscess. The overall mortality rate (death within 30 days of operation) was 4·3 per cent and the morbidity rate was 21·7 per cent.

Recurrent cholangitis and stone formation

The median follow-up period for the 44 patients who survived the operations was 43 months.

Despite repeated dilatation in the five patients treated by dilatation alone (average 2·4 dilatations), all the strictures reformed within 2 months. Cholangitis occurred in two patients and documented recurrent stone formation occurred in one. This patient refused further dilatation or surgery and is still under observation. The patient with successful plastic repair was well on follow-up for over 5 years. Two of the eighteen patients with biliary-enteric anastomosis and two of the twenty patients with liver resection had attacks of cholangitis which subsided with conservative treatment. On investigation no recurrent stone or stricture formation was detected. Thus, good results were obtained in 38 out of 44 patients (86·4 per cent).

Discussion

Many hypotheses have been advanced for the cause of recurrent pyogenic cholangitis. The balance of available evidence firmly indicates that the initiating process is colonization by bowel organisms, via the portal venous system, of the intrahepatic biliary radicals of a patient whose normal defence mechanisms in the liver and biliary tree are compromised by bacterial, parasitic or other toxic substances[1,3]. This, together with poor nutrition, results in precipitation of bilirubinate and stones are gradually formed[1,3,8]. Obstructive cholangitis ensues which leads to further stone formation, biliary stasis and cholangitis and a vicious cycle is established.

In recurrent pyogenic cholangitis, the strictures are inflammatory and they can occur in large or small ducts[1,3].

They are formed by exaggeration of normal healing process excited by transmural ductal injury from infection, the presence of a stone that stimulates continuous tissue overgrowth, and the destruction of liver parenchyma, resulting in loss of external support[1]. Although a history of previous biliary surgery is common, these strictures are unlikely to be the result of iatrogenic injury, the commonest cause of benign biliary stricture in Western countries[9–11]. The left duct is much more commonly affected than the right duct[1–3], strictures are usually short and surrounding fibrosis is not severe, and they can occur in patients without any previous surgical treatment. Furthermore, the strictures are more likely to occur in patients with a long history of repeated cholangitis, suggesting that they are the result of repeated infection[3], while associated strictures in peripheral ducts are common[1,3].

There is still no good explanation why in recurrent pyogenic cholangitis the left duct is earlier and more seriously affected[1–3]. It may be related to the more acute angulation of the left duct as it enters the common hepatic duct, resulting in a less efficient drainage of this side of the biliary system[1,3]. Once strictures are formed, bile duct occlusion leads to hepatic segmental or lobar atrophy due to secondary changes in sinusoidal perfusion by portal venous blood in the chronically obstructed lobe[12]. The left lobe of liver appears more susceptible to atrophy than the right[13]. The reason for this is not clear, although it has been suggested that compression of the left portal vein by dilatation of the long left hepatic duct may be responsible[14].

Definitive surgical procedures should be performed on patients with strictures of the major bile ducts as potential lethal complications are common. Dilatation of strictures with removal of stones is usually followed by restricture formation[4,6], and whether these strictures can be kept patent by repeated dilatation requires a long-term study[4]. In the absence of this information we perform dilatation only on patients who refuse open surgery or who are considered to be at high surgical risk. Hepatotomy and plastic repair are technically difficult and bleeding, bile leakage or restenosis are potential serious complications[1,6]. The reason for failure in plastic repair of diseased ducts is the same as for iatrogenic strictures, namely that after approximation, devitalized denuded duct edges heal by scarring[1]. We have abandoned this procedure because of these potential problems. Hepatic resection is indicated when substantial liver parenchyma in liver segments have been destroyed leaving little more than fibrous sacs containing dilated ducts and stones. Such liver resection is technically easy and may be combined with drainage of the rest of the biliary systems[2,3]. If the left lobe of liver is relatively healthy with stricture at the origin of the left duct, a side-to-side anastomosis of the left duct (exposed by the left duct approach[7]) to a Roux-en-Y loop of jejunum is preferred to left hepatectomy. This is because recurrent pyogenic cholangitis affects the whole liver and it is logical to preserve liver tissues. Furthermore, left hepatectomy is technically more difficult when the liver is relatively healthy. A drainage procedure for the rest of the biliary tree can be performed in these patients if the disease also affects the right lobe of liver. For extrahepatic biliary strictures, biliary-enteric anastomosis between the bile ducts proximal to the strictures to a Roux-en-Y loop of jejunum will provide adequate drainage to the obstructed biliary systems.

The principles in the management of benign inflammatory biliary strictures in recurrent pyogenic cholangitis are the same as in other types of benign biliary structures. If the obstructed liver segments are adequately drained or resected, and all stones are removed, good clinical results can be expected.

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References

1. Wong J. Recurrent pyogenic cholangitis. In: Maingot R, ed. *Abdominal Operations*. 8th edn. New York: Appleton Century Crofts, 1985: 1997–2013.
2. Ong GB. A study of recurrent pyogenic cholangitis. *Arch Surg* 1962; **84**: 199–225.
3. Lam SK, Wong KP, Chan PKW, Ngan H, Ong GB. Recurrent pyogenic cholangitis: a study by endoscopic retrograde cholangiography. *Gastroenterology* 1978; **74**: 1196–1203.
4. Choi TK, Lee MJR, Lui R, Fok M, Wong J. Postoperative flexible choledochoscopy for residual primary intrahepatic stones. *Ann Surg* 1986; **203**: 260–5.
5. Choi TK, Wong J, Lam KH, Lim TK, Ong GB. Late result of sphincteroplasty in the treatment of primary cholangitis. *Arch Surg* 1981; **116**: 1173–5.
6. Choi TK, Wong J, Ong GB. The surgical management of intrahepatic stones. *Br J Surg* 1982; **69**: 86–90.
7. Hepp J, Couinaud C, L'abord et l'utilisation du canal hepatique gauche dans les reparations de la voie biliaire principale. *Presse medicale* 1956; **64**: 947–8.
8. Chou ST, Chan CW. Recurrent pyogenic cholangitis: a necropsy study. *Pathology* 1980; **12**: 415–28.
9. Longmire WP Jr. The diverse causes of biliary obstruction and their remedies: Iatrogenic trauma. *Curr Probl Surg* 1977; **14**: 43–52.
10. Vallon AG, Mason RR, Laurence BH, Cotton PB. Endoscopic retrograde cholangiography in post-operative bile duct strictures. *Br J Radiol* 1982; **55**: 32–5.
11. Bismuth H. Postoperative strictures of the bile duct. In: Blumgart LH, ed. *Clinical Surgery International*. Vol. 5. *The Biliary Tract*. Edinburgh London Melbourne and New York: Churchill Livingstone, 1982: 209–18.
12. Benjamin IS. The obstructed biliary tract. In: Blumgart LH, ed. *Clinical Surgery International*. Vol. 5. *The Biliary Tract*. Edinburgh London Melbourne and New York: Churchill Livingstone, 1982: 157–82.
13. Ham JM. Partial and complete atrophy affecting hepatic segments and lobes. *Br J Surg* 1979; **66**: 333–7.
14. Benz EJ, Baggenstoss AH, Wollaeger EE. Atrophy of the left lobe of liver. *Arch Path* 1952; **53**: 315–30.

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Acute cholangitis in association with acute pancreatitis: incidence, clinical features and outcome in relation to ERCP and endoscopic sphincterotomy

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Although endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) have been shown to be valuable in managing patients with acute cholangitis, their role in patients who have simultaneous acute cholangitis and acute pancreatitis is not known. We have reviewed 32 consecutive patients presenting with both conditions over ten years which represents 23·0 per cent of all cases of gallstone-related acute cholangitis and 14·4 per cent of all cases of biliary acute pancreatitis admitted during the same period. The majority of patients were elderly (median 76 years) and female (75 per cent). Five patients had previously undergone cholecystectomy. Eleven patients were clinically shocked (34 per cent) and blood cultures were positive in 9/14 cases (64 per cent). Twenty patients (63 per cent) had a predicted severe attack of acute pancreatitis (modified Glasgow criteria). Common bile duct (CBD) stones were identified in 15 of 23 patients with successful ERCP. Of these 23 patients, 9 were treated by endoscopic sphincterotomy (ES) alone, 5 by ES and surgery, 4 by surgery alone and 5 were treated conservatively. There was one death (4·3 per cent). Nine patients were managed without cholangiography; four had surgery and five were treated conservatively. There were three deaths (33 per cent; $P = 0.10$*). Evidence of recent CBD stone passage was apparent in eight patients (25 per cent) compared with five out of eighty-seven patients (5·7 per cent) with acute cholangitis alone (*$P < 0.005$*). The results indicate that ERCP and ES may have an important role in the management of these patients.*

Keywords: Cholangitis, pancreatitis, choledocholithiasis, endoscopic retrograde cholangiopancreatography, endoscopic sphincterotomy

Acute cholangitis is a complication which develops in 6–9 per cent of patients with gallstones[1,2]. There is a considerable variation in the clinical severity of the condition with an overall mortality of 10–22 per cent[3–7] although this is 33–65 per cent in the more severe forms of cholangitis[1,8,9].

Acute pancreatitis is known to occur in approximately 8 per cent of patients with gallstones[10]. The frequent finding of gallstones in the faeces of patients with 'biliary' acute pancreatitis[11] and other studies based on surgical exploration of the common bile duct (CBD)[12] or investigation by endoscopic retrograde cholangiopancreatography (ERCP)[13] provide strong evidence that biliary acute pancreatitis is associated with the presence of gallstones in the CBD and/or their passage through the ampulla of Vater. The mortality from biliary acute pancreatitis is reported as varying from around 5 per cent to 20 per cent[14–15].

Despite the association of CBD stones with both cholangitis and pancreatitis the coexistence of these conditions in the same patient has received little comment. It has recently been shown that early endoscopic sphincterotomy (ES) and CBD stone extraction was associated with a significant reduction in mortality from acute cholangitis when compared with operative choledocholithotomy[6]. Whether ERCP/ES is of any value in patients with coexisting acute cholangitis and acute pancreatitis is not known.

The purpose of this study was threefold: firstly, to characterize the clinical and biochemical features of patients with coincidental acute cholangitis and acute pancreatitis; secondly, to analyse the results of ERCP/ES in these patients compared with those patients with acute cholangitis alone; thirdly, to ascertain the relative incidence of coexisting acute cholangitis and acute pancreatitis with respect to each of these conditions alone.

Patients and methods

Thirty-two patients with coexisting acute cholangitis and acute pancreatitis were identified between 1977 and 1986 inclusive. The diagnosis of acute cholangitis was determined on clinical grounds on the basis of jaundice, swinging pyrexia greater than 38°C, pain and tenderness over the liver and rigors and/or the presence of pus in the bile ducts seen at surgery, endoscopic sphincterotomy (ES) or post mortem. The diagnosis of acute pancreatitis was based on a serum amylase greater than 1000 units/litre (Phadebas)[16] in the presence of a compatible clinical picture and/or evidence of acute pancreatitis at surgery or post mortem. Patients were treated with intravenous fluids, parenteral vitamin K and either double IV antibiotic therapy with a cephalosporin (cephradine, cefazolin or cefuroxime) and metronidazole or triple IV therapy with penicillin, gentamicin and metronidazole.

The predicted severity of the attack of acute pancreatitis was determined using eight of the Glasgow criteria[17] including age greater than 55 years, but excluding a serum alanine transaminase greater than 200 units/litre (*Table 1*). ERCP was performed using a standard technique as previously described but pancreatography was avoided if

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Table 1 *Criteria used to predict severity of attack of acute pancreatitis**

Age > 55 years	Albumin < 32 g/l
WCC > 15 × 10⁹/l	Calcium < 2·0 mmol/l
Urea > 16 mmol/l	P_{a,O_2} < 8 kPa
Glucose > 10 mmol/l	LDH > 600 units/l

* Predicted mild attack, 0–2 factors; predicted severe attack, 3–8 factors

possible[6]. If CBD stones were identified at ERCP, ES was performed with a positive stone extraction policy[6].

Ten patients underwent serial computerized tomography (CT) from July 1984. CT scans were performed on admission, at 1 week and at 6 weeks using an IGE 8800 scanner. On the first scan contrast enhancement was employed by administering 50 ml of Niopam given slowly intravenously. All scans were reported blind by a single consultant radiologist.

The incidence of acute pancreatitis was determined in a consecutive group of patients with acute cholangitis from gallstones presenting to the Leicester Hospitals (850 000 catchment population) from 1977 to 1985 inclusive. This was achieved in the main by retrospective analysis of over 2500 case notes. The incidence of acute cholangitis in a consecutive group of patients with acute pancreatitis from gallstones presenting to the Leicester Royal Infirmary between 1980 and 1986 inclusive was determined prospectively.

Clinical and laboratory results were compared with the group of patients presenting with acute cholangitis alone. Outcome was related to the initial presentation and whether or not ERCP/ES was employed.

The two-tailed Mann–Whitney Ranking Test was used to analyse continuous parameters (Minitab Computer Package) and the χ^2 test was used to analyse discrete clinical variables. The χ^2 test with Yates' correction was used when the expected number of observations was small.

Results

Clinical, biochemical and radiological features

There were 24 women and 8 men. The median age was 76 years (range 52–87 years). Five patients had undergone previous cholecystectomy at between 6 months and 7 years previously. All but one of the patients was jaundiced. Eleven of the patients (34 per cent) were clinically shocked on admission (systolic BP < 100 mmHg). The haematological and biochemical values for the patients are summarized in *Table 2* and are compared with 87 patients presenting with acute cholangitis alone. Blood cultures were taken in 14 patients before antibiotic therapy was started and one or more organism was grown in nine patients (64 per cent). The types of organism grown are shown in *Table 3*. One patient with negative blood cultures developed distant focal sepsis (lumbar osteitis).

Twenty patients (63 per cent) were predicted as having a severe attack of acute pancreatitis with a median score of 4·0 (range 3–6). Twelve patients were predicted as having a mild attack with a median score of 1·5 (range 1–2). Only one patient was aged under 55 years and this was a patient with a severe attack (score = 4). The presence of acute pancreatitis was confirmed by means other than clinical criteria in 16 patients: in 8 patients this was by CT alone, in 2 patients by CT and early surgery and in 5 patients by early surgery alone, and in 1 patient this was at post-mortem examination.

Treatment and outcome

ERCP was attempted in 24 patients and was successful in 23 but failed in 1 who had previously undergone a Polya partial gastrectomy (*Figure 1*). ERCP was undergone by 9 patients (7 predicted severe) at 1–3 days and by 14 patients (6 predicted severe) at 5–28 days. CBD stones were confirmed in 15 patients, and ES was successfully undertaken and stones removed in all 14 patients in whom this was attempted; the remaining patient had an uneventful cholecystectomy and successful choledocholithotomy. Complications attributable to ERCP/ES occurred in two patients, both following CBD stone extraction: one developed an exacerbation of acute cholangitis and the other developed lumbar osteomyelitis. Thus the overall complication rate of ERCP was 8 per cent or 14 per cent following ES.

Of the 23 patients who had ERCP/ES, 5 had major systemic complications on admission but all 5 improved following ES and CBD stone extraction. In two cases this was followed by planned surgery to deal with septic complications of the liver, gallbladder and pancreas. Seven other patients also underwent cholecystectomy following resolution of the acute cholangitis/pancreatitis (*Figure 1*). Nine patients were discharged home following ES alone, eight with gallbladder *in situ* who were considered unfit for surgery (one of the latter was found to have a clinically insignificant pseudocyst on the CT scan at 6 weeks). Five patients without confirmed CBD stones were also not subjected to surgery because of their poor condition. One patient died 3 weeks after a normal ERCP from a cerebrovascular accident. None of those patients discharged home have had further problems from cholangitis or pancreatitis, nor from cholecystitis in those with gallbladder *in situ*.

Nine patients were treated by conventional means (*Figure 1*). Four patients had major complications on admission, of whom two died. One died without surgery and was found to have pus in the bile ducts and severe haemorrhagic pancreatitis. The other patient presented with a perforated gallbladder and died soon after surgery, involving cholecystectomy and choledocholithotomy with T-tube insertion, from cardiorespiratory failure. A fifth patient who was relatively well on admission died after cholecystectomy and a *negative* exploration of the CBD, from postoperative cardiorespiratory failure. Only four patients in

Table 2 *Important biochemical features* of the 32 patients with acute cholangitis and acute pancreatitis. For comparison the biochemical features of 87 other patients with acute cholangitis are also shown*

	Acute cholangitis and acute pancreatitis ($n = 32$)	Acute cholangitis only ($n = 87$)
Amylase (units/l)	2940 (1120–10 848)	160 (19–840)
White cell count† (× 10⁹/l)	15·9 (1·2–51·9)	12·7 (4·0–31·0)
Urea (mmol/l)	6·7 (2·6–28·7)	6·9 (1·9–56·5)
Blood sugar (mmol/l)	7·8 (2·1–36·1)	6·6 (1·4–19·8)
P_{a,O_2} (kPa)	9·7 (4·0–14·1)	—
Calcium (mmol/l)	2·11 (1·31–2·46)	—
Lactate dehydrogenase (units/l)	445 (252–842)	—
Alkaline phosphatase (units/l)	407 (97–2365)	463 (29–2178)
γ-Glutamyl transpeptidase (units/l)	465 (86–1110)	357 (39–1926)
Alanine transaminase (units/l)	171 (36–614)	134 (12–895)
Bilirubin (μmol/l)	105 (8–240)	114 (20–379)
Total protein (g/l)	60·5 (50–76)	62·0 (47–83)
Albumin (g/l)	31·5 (22–44)	32·0 (22–47)

* Median values (range in parentheses)

† All differences are not statistically significant ($P > 0·05$) with the obvious exception of amylase and also the white cell count ($P = 0·0272$) using the Mann–Whitney *U* test

Table 3 *Types of organism grown from blood cultures in nine out of fourteen patients with acute cholangitis and acute pancreatitis*

Organism	Number
Escherichia coli	5
Proteus mirabilis	2
Klebsiella pneumoniae	1
Bacteroides fragilis	1
Streptococcus faecalis	1
Streptococcus viridans	1
Staphylococcus albus	1

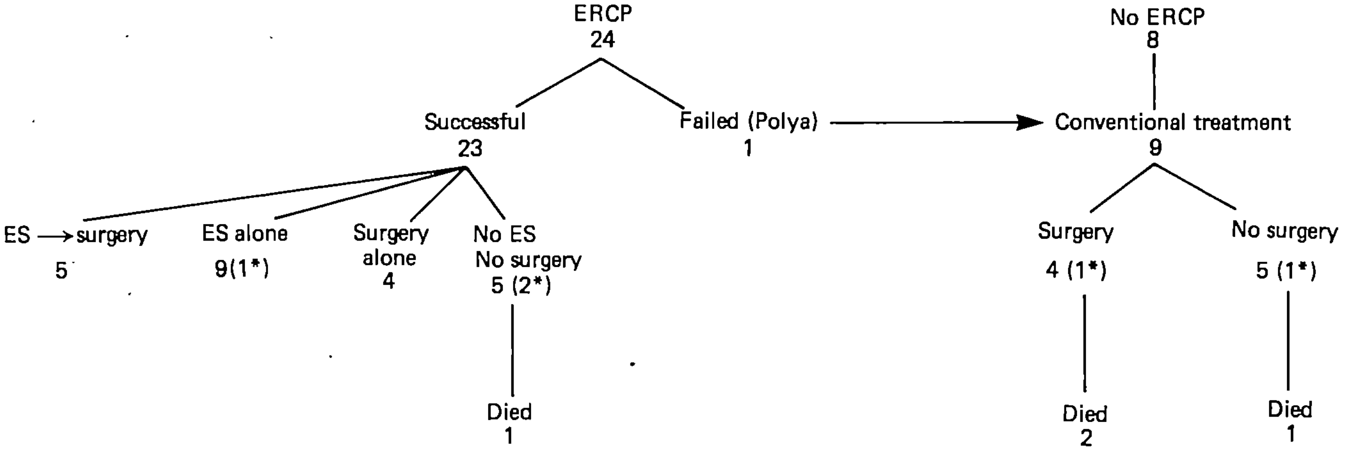

Figure 1 *Outcome in 32 patients with acute cholangitis and acute pancreatitis in relationship to ERCP and type of treatment received. *Five patients had undergone previous cholecystectomy*

Table 4 *Clinical features and outcome in patients with acute cholangitis and acute pancreatitis compared with patients with acute cholangitis only*

Patient characteristics	Acute cholangitis and acute pancreatitis ($n=32$)	Acute cholangitis only ($n=87$)
Median age (range) years	76 (52–87)	74 (25–88)
Females/males	24:8 (75%)	55:32 (63%)
Positive blood culture	9/14 (64%)	34/60 (57%)
Previous cholecystectomy	5 (15·6%)	7 (8·0%)
ERCP	24 (75%)	60 (69%)
Passed CBD stones*	8 (25%)	5 (5·7%)
ES performed	15 (47%)	40 (46%)
All deaths	4 (12·5%)	13 (14·9%)

*This difference was statistically significant ($\chi^2=8{\cdot}912$, d.f.$=1$, $P=0{\cdot}0028$); none of the other differences were significant

this group underwent surgery with common bile duct exploration, so the number of patients in this group who had stones (or passed them) could not be properly established.

Overall, complications occurred in 11 out of 20 patients predicted as severe (55 per cent) compared with only 2 out of 12 predicted mild (17 per cent; $\chi^2=3{\cdot}12$, d.f.$=1$, $P=0{\cdot}0768$). The difference in mortality between those treated conventionally (33 per cent) and those treated by ERCP/ES (4·3 per cent) was not statistically significant ($\chi^2=2{\cdot}67$, d.f.$=1$, $P=0{\cdot}10$).

Incidence of CBD stones

Overall, CBD stones were retrieved in 19 patients at variable times following admission (in 14 by ES, in 4 by surgery and in 1 at post mortem). In eight other cases there was evidence that CBD stones had passed spontaneously. CBD stones were shown by intravenous cholangiography in one patient and by ultrasonography (US) in two other patients. Six patients with empty main bile ducts at ERCP, had a gaping papilla of Vater (as well as a dilated CBD) indicating recent stone passage. One of the latter six patients was also shown to have a large CBD stone by US: a 7-day swinging pyrexia of up to 40°C abruptly resolved and ERCP a few days later revealed an open papilla indicating spontaneous CBD stone passage.

Stones from the CBD were retrieved in all but five patients who had acute cholangitis alone. The passage of CBD stones was determined by the findings at ERCP in three and by surgery and post-mortem examination in one case each.

Incidence relative to all cases of acute cholangitis or acute pancreatitis

From the 9-year retrospective analysis 113 cases of acute cholangitis due to gallstones were identified, and 26 of these also had acute pancreatitis (23·0 per cent). For comparison the clinical features and outcome in all patients with acute cholangitis with and without pancreatitis are shown in *Table 4*. From the 7-year prospective study of acute pancreatitis, there were 316 cases with various aetiologies: 187 of these patients were found to have gallstones, of whom 27 also had acute cholangitis (14·4 per cent).

Discussion

In this study Charcot's triad (jaundice, swinging pyrexia >38°C and liver tenderness) was used as the basis for diagnosing acute cholangitis. Some authors have defined acute cholangitis as a fever >38·3°C *or* a history of rigors in the presence of CBD stones[18] but we would consider this too liberal a definition. Similarly we would not accept that over 20 per cent of patients are not clinically jaundiced[3] at the time of diagnosis. In the present study all but one of the patients was jaundiced. The incidence of positive blood cultures was 64 per cent in those in whom these were undertaken, or 28 per cent of all patients. The respective figures for acute cholangitis alone previously reported are around 40 per cent (range 25–65 per cent) and 25 per cent (range 5–65 per cent)[1–7]. Clinical shock was apparent in 34 per cent of patients in this series. This compares with previous reports of 7–25 per cent for acute cholangitis alone[4,6,7] and a similar incidence of 33 per cent was reported only by Hinchey and Couper in 24 cases of severe ('suppurative') acute cholangitis[9]. Patients with acute cholangitis and acute pancreatitis were similar in age (median 76 years) compared with patients with acute cholangitis alone from this centre (median 74 years). In contrast, studies of patients with acute cholangitis alone from other centres have indicated younger groups of patients (range of mean ages 47–61 years)[4,5,7].

Sixty-three per cent of the patients with acute cholangitis and acute pancreatitis had scores predictive of a severe attack of acute pancreatitis. In the absence of acute cholangitis, only approximately 30 per cent of patients, however, would be expected to have scores predicting a severe attack, using the Glasgow criteria[17,19].

Only 5·7 per cent of patients with acute cholangitis alone had evidence of stone passage through the ampulla of Vater, compared with 25 per cent of patients who, in addition, had acute pancreatitis ($P<0{\cdot}05$). This supports the theory that it is the passage of relatively small stones which is important in the initiation of acute pancreatitis[10,12]. On the the other hand, persisting CBD stones may promote the development of acute cholangitis and, indeed, may also be an important factor in prolonging the attack of acute pancreatitis.

Although ERCP and ES have been shown to be effective in a variety of clinical situations, their use in acute conditions has yet to receive wide support. Indeed the use of ERCP and ES has been vehemently condemned in the presence of either acute cholangitis or acute pancreatitis[20]. Recently it has been shown that early ES and stone extraction in patients with acute cholangitis significantly improved mortality (4·7 per cent) when compared with early surgical decompression (21·4 per cent)[6]. The safety and effectiveness of ERCP and ES have also been shown in a recent prospective randomized study involving patients with biliary acute pancreatitis[19], supporting the good results shown in previous uncontrolled studies[21,22].

In the present study of patients with both conditions, the numbers are too small to draw statistical significance regarding outcome between those undergoing ERCP/ES and those treated by conventional means. Nevertheless, we believe that there are benefits: ERCP revealed CBD stones in 15 patients and prompted their endoscopic extraction in 14 of these; ERCP also showed that CBD stones had been passed in 8 others and this was also important as it supported continued conservative management. Whether or not ES should be performed in all of these patients, irrespective of the presence or absence of CBD stones, is still an open question.

The use of ES should be regarded as an adjunct to conventional treatment. Given the age and frailty of these patients, some of them may not be suitable for cholecystectomy following ES—indeed, none of the patients discharged home has sustained further attacks of pancreatitis or cholangitis. One of the three patients who died in the conventionally treated group would almost certainly have benefited from early ERCP by revealing CBD stone passage and thereby removing the main indication for surgery in this case. Emergency surgery was the correct approach in the patient with a perforated gallbladder who subsequently died. Although ES may have been of benefit to the third patient who died in this group, the diagnosis was made only at post-mortem examination.

The incidence of acute pancreatitis in a consecutive series of gallstone-related acute cholangitis in this study was 23·0 per cent. Although this figure may seem unduly high, it would represent on average only one case (or less) presenting to an average-sized district hospital per year. Acute pancreatitis complicating cholangitis has not previously gone unnoticed. Andrew and Johnson reported an incidence of 24 per cent in 17 patients with acute 'suppurative' cholangitis diagnosed at urgent laparotomy or post mortem but the relevance of this association was not discussed[1]. In this latter study the diagnosis was based on gross pathology; the wider availability of CT scanning should allow the diagnosis of acute pancreatitis to be more commonly confirmed in patients with a high amylase[23] irrespective of the presence of acute cholangitis.

The incidence of acute cholangitis in a consecutive series of patients with biliary pancreatitis was 14·4 per cent in this series. McMahon *et al.* reported seven instances of acute cholangitis (with three deaths) out of 459 cases of all types of acute pancreatitis (1·5 per cent *versus* 8·5 per cent in this series)[24]. As these data were derived from a study of peritoneal lavage in the treatment of acute pancreatitis involving 24 hospitals, accurate documentation of all the features of cholangitis may have proved difficult[25].

On the basis of these results and taken in conjunction with other studies[6,19,21,22], we can confidently recommend the use of ERCP/ES in patients with acute cholangitis irrespective of whether acute pancreatitis is an additional feature. We stress, however, that the use of ERCP/ES should be considered an adjunct to conventional means of management, including surgery, and should not be regarded as an absolute alternative.

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References

1. Andrew DJ, Johnson SE. Acute suppurative cholangitis, a medical and surgical emergency. *Am J Gastroenterol* 1970; **54**: 141–54.
2. Saik RP, Greenburg AG, Farris JM, Peskin GW. Spectrum of cholangitis. *Am J Surg* 1975; **130**: 143–50.
3. Boey JH, Way LW. Acute cholangitis. *Ann Surg* 1980; **191**: 264–70.
4. Lygidakis NJ. Acute suppurative cholangitis: comparison of internal and external biliary drainage. *Am J Surg* 1984; **143**: 304–6.
5. Saharia PC, Cameron JL. Clinical management of acute cholangitis. *Surg Gynecol Obstet* 1976; **142**: 369–72.
6. Leese T, Neoptolemos JP, Baker AR, Carr-Locke DL. Management of acute cholangitis and the impact of endoscopic sphincterotomy. *Br J Surg* 1986; **73**: 988–92.
7. Thompson JE, Tompkins RK, Longmire WP. Factors in management of acute cholangitis. *Ann Surg* 1982; **195**: 137–45.
8. Haupert AP, Carey LC, Evans WE, Ellison EH. Acute suppurative cholangitis. *Arch Surg* 1967; **94**: 460–8.
9. Hinchey EJ, Couper CE. Acute obstructive suppurative cholangitis. *Am J Surg* 1969; **117**: 62–7.
10. Armstrong CP, Taylor TV, Jeacock J, Lucas S. The biliary tract in patients with acute gallstone pancreatitis. *Br J Surg* 1985; **72**: 551–5.
11. Acosta JM, Ledesma CL. Gallstone migration as a cause of acute pancreatitis. *N Eng J Med* 1974; **290**: 484–7.
12. Stone HH, Fabian TC, Dunlop WE. Gallstone pancreatitis: biliary tract pathology in relation to time of operation. *Ann Surg* 1981; **194**: 305–10.
13. Neoptolemos JP, London N, Bailey I, Shaw D, Carr-Locke DL, Fossard DP, Moossa AR. The role of clinical and biochemical criteria and endoscopic retrograde cholangiopancreatography in the urgent diagnosis of common bile duct stones in acute pancreatitis. *Surgery* 1986; **100**: 732–43.
14. Corfield AP, Cooper MJ, Williamson RCN. Acute pancreatitis: a lethal disease of increasing incidence. *Gut* 1985; **26**: 724–9.
15. Goodman AJ, Neoptolemos JP, Carr-Locke DL, Finlay DBL, Fossard DP. Detection of gallstones after acute pancreatitis. *Gut* 1985; **26**: 125–32.
16. Leska M, Birath K, Brown B. A new and rapid method for the clinical determination of alpha-amylase activities in human serum and urine. *Clin Chim Acta* 1969; **26**: 437–53.
17. Blamey SL, Imrie CW, O'Neill J, Gilmour WH, Carter DC. Prognostic factors in acute pancreatitis. *Gut* 1984; **25**: 1340–6.
18. Pitt HA, Postier RG, Cameron JL. Consequences of preoperative cholangitis and its treatment on the outcome of operation for choledocholithiasis. *Surgery* 1983; **94**: 447–52.
19. Neoptolemos JP, London N, Slater ND, Carr-Locke DL, Fossard DP, Moossa AR. A prospective study of ERCP and endoscopic sphincterotomy in the diagnosis and treatment of gallstone acute pancreatitis. *Arch Surg* 1986; **121**: 697–702.
20. Pitt HA. Is endoscopic sphincterotomy a safe and effective method for the management of stones in the distal common bile duct? In: Gitnick G, ed. *Controversies in Gastroenterology.* London: Churchill Livingstone, 1984: 89–116.
21. Safrany L, Cotton PB. A preliminary report: urgent duodenoscopic sphincterotomy for acute gallstone pancreatitis. *Surgery* 1981; **89**: 424–8.
22. Rosseland AR, Solhaug JH. Early or delayed endoscopic papillotomy (EPT) in gallstone pancreatitis. *Ann Surg* 1984; **199**; 165–7.
23. London ND, Neoptolemos JP, Bailey I, James R. Serial CT scanning in acute pancreatitis (abstract). *Gut* 1987, in press.
24. McMahon MJ, Mayer AD, Shearer MG *et al.* Cholangitis and acute pancreatitis (abstract). *Gut* 1985; **26**: A648.
25. Mayer AD, McMahon MJ, Corfield AP *et al.* Controlled clinical trial of peritoneal lavage for the treatment of severe acute pancreatitis. *N Engl J Med* 1985; **312**: 399–404.

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Ureteric re-implantation in the neuropathic bladder

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During the last 5 years 174 children with neuropathic bladder were studied, and only 7 required urinary diversions. A total of 31 ureteroneocystostomies were performed in 17 patients, 16 of whom had gross vesico-ureteric reflux. Revisionary surgery was required in four children and two underwent pyeloplasty. Deterioration followed ureteroneocystostomy in two patients, but 13 (76 per cent) of the children were significantly improved

Keywords: Vesico-ureteric reflux, ureteroneocystostomy, intermittent catheterization, neuropathic bladder

A major cause of morbidity and mortality in children with neuropathic bladder is ascending infection causing chronic pyelonephritis[1]. This may be secondary to vesico-ureteric reflux (reflux), which occurs in up to a third of patients[2]. Such reflux may be reduced in severity by judicious bladder management[3–6], but a quarter to a third of children with neuropathic bladder accompanied by reflux suffer progressive deterioration of the upper tracts requiring additional measures[5–7]. In the past, ileal diversion was commonly used to protect the upper tracts but it is replete with complications[8] and the long-term results are poor[6,9,10]. An alternative approach involves ureteroneocystostomy (re-implantation) combined with procedures to improve bladder emptying[5] and storage capacity. Until recently, re-implantation was considered to be difficult to perform, to be associated with high complication rates, and to confer little benefit[11,12]. Provided the neuropathic bladder is regularly emptied, we believe that ureters can be re-implanted successfully, and support our contention with the following series.

Patients and methods

During the 5-year period from December 1980 to December 1985, 174 children with neuropathic bladder were managed by a single surgical unit. This group consisted of 132 regularly attending survivors from a series of 265 neonates treated by the unit over 20 years plus 42 older children referred after initial treatment elsewhere. Several of the latter group had delayed onset of incontinence caused by spina bifida occulta.

In the first 2 years of the survey, five children suffered upper tract deterioration progressing to renal failure and underwent urinary diversion by cutaneous ureterostomy, but since 1981 no neuropathic bladder has been abandoned. The majority of the children over the age of 5 years were being intermittently catheterized[13] although 11 severely disabled older children had an indwelling catheter, 13 had an ileal diversion, 26 were in nappies, 6 had a penile appliance—only 14 had normal micturition. All of the children underwent regular assessment of the urinary tract. Those with an undiverted system and recurrent infection or upper tract dilatation were submitted to micturating cystourethrography (MCU). All children (8 girls and 8 boys) with reflux in grades III to V in the International Study Classification[14] underwent re-implantation. Bilateral reflux was demonstrated in only two of these children. Before re-implantation, seven of the sixteen children were in nappies, four were intermittently catheterized and five had an indwelling catheter. Lesser grades of reflux were infrequently encountered because repeat MCU was rarely performed in the absence of deteriorating upper tracts. Minor grades of reflux were an indication to institute intermittent catheterization or to increase the frequency of catheterization.

Bladder neuropathy was secondary to myelomeningocoele in 15 patients and followed resection of a neonatal sacrococcygeal teratoma in one girl. All of these children suffered recurrent urinary tract infection. Another girl with anorectal agenesis and incontinence attributed to a neuropathic bladder secondary to sacral agenesis underwent cystoscopic examination which demonstrated a single, ectopic, non-refluxing hydro-ureter which was implanted into the bladder. Cystoscopy was performed in 11 patients with reflux, 5 of whom had bilateral patulous (golf-hole) ureteric orifices despite having only unilateral reflux demonstrated on MCU. The non-refluxing ureter had a normal orifice in two children and one had a solitary golf-hole ureteric orifice. The ureteric orifices could not be seen in two patients because of marked trabeculation, which was present to some extent in all of the children. Only one patient with bilateral reflux underwent cystoscopic examination which revealed one patulous and one normal ureteric orifice.

Renal function was assessed by blood chemistry (plasma urea, electrolytes and creatinine) and by glomerular filtration rate (GFR) calculated by computer from ^{99m}Tc-diethylene triamine pentacetic acid (DTPA) isotope studies[15]. When infection free, all of the children had normal levels of plasma creatinine, although the majority had levels at the top end of the normal range for their age group. It was common for them to have transient rises in plasma creatinine during attacks of urinary tract infection. Urinary tract dilatation and scarring were assessed by intravenous urography or by ultrasound examination and ^{99m}Tc-dimercaptosuccinic acid (DMSA) imaging[15]. Scars were detected in 20 of the 32 kidneys.

Manometric studies were not performed because a decision had been made that long-term pharmacological manipulation would not be used and that bladder emptying would be controlled with a catheter, providing 'dryness', when necessary, by increasing bladder outlet resistance with various surgical procedures.

The Leadbetter–Politano technique[16] of re-implantation was used in 16 children. In addition, in five with a mega-ureter, a nipple valve was fashioned at the site of the new ureteric orifice[17,18]. The Ahmed–Cohen advancement method[19] was used in one child. Where both kidneys were present, bilateral re-implantation was carried out except in a 15-year-old boy in whom a decision was made not to re-implant the unaffected ureter after technical difficulties had been experienced with the refluxing ureter. Postoperatively, ureteric stents were kept in place for 7 days and a suprapubic catheter for 10 days. The age at re-implantation varied from 6 months to 15 years (mean 6·7 years ± 4·5).

Renal ultrasound examination was performed 3 months after re-implantation and repeated approximately every 6–12 months thereafter. All of the children had at least one postoperative DTPA or DMSA scan, repeated every 2 years, and a MCU performed 6 months after re-implantation. Urine cultures were performed regularly at the clinic but antibiotic treatment was recommended only in the presence of symptomatic infection.

The success of surgery was assessed by control of reflux, reduction in upper tract dilatation, decreased incidence of urinary tract infection and improvement in renal function and general health.

Results

Two months after operation, one boy died suddenly from a blocked cerebrospinal fluid shunt associated with an undiagnosed mid-brain glioma. For convenience, a general practitioner referred a 15-year-old boy to another hospital where the urologist performed an ileal diversion without reference to his previous treatment. The other 15 children have been regularly reviewed over a period of between 1 and 5 years (mean 3·9 years ± 1·3).

During the first few weeks after re-implantation, ultrasound examination demonstrated transiently increased hydro-

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nephrosis in several patients, but after a delay of 6 months or more, the degree of dilatation was less than before operation in all but seven upper tracts in five children. This improvement was maintained throughout the duration of follow-up. After additional surgery, another four upper tracts improved. Plasma creatinine levels frequently rose during the first few days after operation but returned to normal levels within 8 days except in three of the five children with complications. Even in this group the results returned to normal following further treatment. At the time of review, none of the children had a glomerular filtration rate less than that before operation and, in the seven for whom more than two serial results were available, four had developed an increased glomerular filtration rate as would be expected with renal growth and development, and three had results which remained within the normal range for their ages. Since the GFR is calculated within a few seconds of the injection of the isotope, the result is unaffected by the cessation of reflux.

A solitary kidney was present in two of the children, but all of the others underwent bilateral re-implantation, providing a total of twenty-eight renal units for review (*Table 1*). Both of those with bilateral reflux had bilateral upper tract dilatation which improved after re-implantation. Of the two children with solitary systems, one had a dilated, non-refluxing, ectopic ureter before operation, and one had a dilated refluxing right ureter. Both improved after re-implantation. Unilateral reflux and ipsilateral dilatation was present in six cases and four improved after the first operation. Reflux persisted in two patients, both of whom finally had an excellent result after revisionary re-implantation. Five children had unilateral reflux but bilateral upper tract dilatation before operation and this group did less well than the others. Improvement followed re-implantation in three, although one has severe scarring of the previously refluxing system and another required pyeloplasty of both elements of a crossed, fused, ectopic kidney. Two boys have done badly. One continued to deteriorate for 18 months after surgery and then underwent bilateral revisionary re-implantation for vesico-ureteric obstruction. This was followed by improvement and the kidneys returned to a degree of hydronephrosis similar to that seen before the original operation. Fortunately, the reflux was controlled, his general health improved and he had fewer symptomatic infections. The other boy has severe handicaps from a thoracolumbar myelomeningocele accompanied by gross kyphoscoliosis which would have made the application of an abdominal urine collecting device impossible. There was a calculus in the left, non-refluxing system. Following bilateral re-implantation, the stone continued to grow and the previously refluxing right ureter dilated considerably. The obstructed right ureter was then anastomosed to the re-implanted left ureter and improvement followed. Therefore, three renal units deteriorated after re-implantation, one had continued growth of a calculus, and 24 (86 per cent) kidneys had a persistently normal appearance or reduced hydronephrosis. Of course, clubbed calyces and scars remained in all affected kidneys, but none of the kidneys developed new scars during the period of review.

Nipple re-implantation was performed on five hydro-ureters in five children, of whom one subsequently underwent ileal diversion, two progressed satisfactorily, and two required re-operation for persistent reflux. When compared to the standard Leadbetter–Politano re-implant, the nipple re-implants had a poor success rate, but the difference was not statistically significant ($\chi^2 = 1{\cdot}015$, $P > 0{\cdot}10$).

Following re-implantation, four children reverted to almost normal micturition, eight were managed with clean intermittent catheterization, and two with an indwelling urethral catheter. The kyphoscoliotic boy with high-level paraplegia had an indwelling catheter inserted through a perineal urethrostomy to protect the pendulous urethra. This boy, and a girl, underwent bladder neck suspension to the pubis, and one girl had a V–Y narrowing of the bladder neck at the time of re-implantation. All can be kept dry without medication, but the irrational mother of one girl occasionally abandons the catheter and then her daughter is incontinent.

It was difficult to be sure of the number of urinary tract infections suffered by these children, many of whom were treated with antibiotics, without the benefit of bacteriological studies, by their general practitioners, school doctors and local accident service doctors. As far as we can ascertain, all had fewer symptomatic infections after re-implantation, but it would be unreasonable to attempt to support this claim with dubious statistics.

Discussion

Aetiology of vesico-ureteric reflux in the neuropathic bladder is unclear but is probably related to chronic infection, to the presence of sacculations in the vicinity of the ureteric orifices[2,20,21] and to some degree of detrusor–sphincter dyssynergia all preventing ureteric valve closure by the trigonal musculature during detrusor contraction[22–24]. Almost all of the

Table 1 *Outcome of treatment in relation to type of abnormality*

Type of abnormality	Number of children	Outcome expressed as individuals	Outcome expressed as renal units
Bilateral reflux			
Bilateral upper tract dilatation	2	2 improved	4 improved
Unilateral reflux			
Dilated solitary system	2	2 improved	2 improved
Ipsilateral system dilated: contralateral system normal	6	4 improved	4 improved 4 remained normal
		2 improved following reoperation for persistent reflux and 1 also had a pyeloplasty for secondary PUJ obstruction	2 improved 2 remained normal
Bilateral upper tract dilatation	5	2 improved	4 improved
		1 improved after pyeloplasty of both elements of cross-fused ectopic kidney for secondary PUJ obstruction	2 improved
		2 poor results: both reoperated for vesico-ureteric obstruction	2 temporarily deteriorated 1 residual calculus 1 deteriorated
Total	15	13 improved 2 poor results	18 improved 6 remained normal 4 deteriorated

PUJ, pelvi-ureteric junction

children have some degree of static or dynamic distal sphincter obstruction[11,22]. Trabeculated bladders and thick-walled hydro-ureters present technical difficulties which may cause severe complications after re-implantation. For these reasons, the advisability of ureteroneocystostomy in the neuropathic bladder has been questioned, especially as the operation was thought to do little to cure aetiological abnormality, thereby resulting in postoperative reflux[25]. Indeed, before popularization of clean intermittent catheterization in 1972[13], the results of re-implantation were poor[5,11,26].

It is known that gross reflux from the neuropathic bladder seldom improves spontaneously during infancy[5,7,20,21,23] and in our experience there is a marked tendency to deterioration with ageing. Many authorities have come to rely upon frequent emptying of the bladder by intermittent catheterization[5,6,13,23,24] to control the reflux, but this may fail in 10–30 per cent of patients[7] and some of these progress to rapid renal failure because of infection potentiated by insertion of the catheter[12,21]. Then it is necessary either to perform a diversionary operation[11] or to render the patient incontinent by sphincterotomy, to be followed by application of an external collecting device[11,23,27] or by insertion of an expensive artificial sphincter[28]. External sphincterotomy does not always cure reflux[20,21,27] and the possibility of increased incontinence is unacceptable to many patients[24]. We suspect that some of the antagonism to re-implantation stemmed from the widespread acceptance of ileal diversion during the period 1960–1975 and a reluctance to abandon what was seen as the treatment of choice for the neuropathic bladder[11,24]. Now that the long-term complications of ileal diversion have been reported[9,10], it is clear that the procedure is unsafe and ineffective, and in those with severe kyphoscoliosis the external collecting device often becomes detached causing wetness and psychological depression. Therefore, we decided to preserve the bladders of our patients as natural internal reservoirs and, if necessary, to provide 'dryness' by increasing the bladder outlet resistance, to facilitate bladder emptying by catherization, and to prevent reflux by ureteric re-implantation.

In unilateral refluxers undergoing cystoscopic examination, the incidence of bilateral patulous ureteric orifices was about 50 per cent, suggesting that up to half of the patients would develop reflux in the initially 'normal' ureter[12,26,29]. It seemed prudent to re-implant both ureters simultaneously rather than to risk having to reoperate in a scarred field with all its attendant risks; but we have no firm evidence that this was a wise decision[5,21]. Re-implantation of the non-refluxing ureter caused deterioration in only one upper tract in a boy in the poor risk group with unilateral reflux and bilateral hydronephrosis.

Re-implantation of the ureters interferes with the trigonal musculature and in some mysterious way may improve bladder emptying in some patients. Postoperatively, four of our patients developed almost normal control, without the need for pharmacological help or catheterization[21]. In the absence of regular, spontaneous micturition, it is essential to ensure frequent and complete bladder emptying by other means so as to prevent surges in intravesical pressure[5]. Intermittent catheterization was well tolerated by over 80 per cent of the children unable to void spontaneously, but it does not suit all children and adolescents[6,24,30]. Parents of two infant boys in this series could not cope with urethral catheterization, so both were provided with a temporary vesicostomy until able to catheterize themselves[6,24,31]. An older boy with severe handicaps had an indwelling catheter passed through a perineal urethrostomy[7]. For re-implantation combined with intermittent catheterization, recent authors[5,21,24,31–33] have had success rates of 85–100 per cent, with few reported complications, although many of the patients had little bladder trabeculation or had the outlet resistance decreased by urethral dilatation, external sphincterotomy, pharmacological manipulation, or Y–V plasty. Our results and complications are similar to those of Johnston *et al.*[12], four of our patients requiring reoperation, two because of persistent reflux which was then cured, and two because of obstruction. The former pair had mega-ureters re-implanted by one of the nipple techniques[17,18]—operations we have abandoned in favour of tailoring or long tunnel re-implantation[12,21,34]. It is important to avoid high re-implantation because of the inherent risk of ureteric obstruction and it is better to do a low re-implant with advancement onto the trigone or to use the Cohen–Ahmed cross-over technique[12,21,26,31,34]. When ventrosuspension of the urethra is to be performed experience with patients, other than in this series, suggests that it may be advisable to re-implant medially, across the posterior wall of the bladder to avoid obstruction of an advanced ureter.

For the neuropathic bladder, most experts[6,24,30] agree that there is no single treatment that is completely effective and without significant complications, but we consider our chosen method of management to be as effective as most and without the major problems associated with the use of an artificial sphincter[5,6,28]. We accept that it is controversial to increase outlet resistance in children with severe reflux and hydronephrosis[11,23] but believe our results to be no worse than those of diversions. However, the selection of cases remains a problem[21,25] and experience with ileal diversion suggests that caution should be expressed with regard to the longterm results of any method of management of the neuropathic bladder in children[21,31,34].

In the 10 per cent of children with neuropathic bladder in whom gross vesico-ureteric reflux threatens the upper tracts, we conclude that anti-reflux surgery is preferable to diversion. Severe reflux seldom ceases spontaneously and catheterization combined with re-implantation is successful in the majority of patients[35], although in the future, open surgery for the correction of reflux may be superseded by the endoscopic injection of pyrolysed polytetrafluoroethylene paste[36].

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References

1. Lister J, Zachary RB, Brereton RJ. Open myelomeningocoele–A ten year review of 200 consecutive closures. In: Rickham PP, Hecker WCh, Prevot J, eds. *Progress in Paediatric Surgery Vol X*. Baltimore–Munich: Schwarzenberg, 1977, 161–77.
2. Kaplan WE, Firlit CF. Management of reflux in the myelodysplastic child. *J Urol* 1983; **129**: 1195–7.
3. Bauer SB, Colodny AH, Retik A. Management of children with vesico-ureteric reflux and myelodysplasia. *J Urol* 1982; **128**: 102–5.
4. Snyder HMcC III, Kalichman MA, Charney E, Duckett JW. Vesicostomy for neurogenic bladder with spina bifida: follow-up. *J Urol* 1983; **130**: 724–6.
5. Kass EJ, Koff SA, Diokno AC. Fate of vesicoureteral reflux in children with neuropathic bladders managed by intermittent catheterization. *J Urol* 1981; **125**: 63–4.
6. Cass AS, Luxenberg M, Johnson CF, Gleich P. Management of the neurogenic bladder in 413 children. *J Urol* 1984; **132**: 521–5.
7. El Gohary A, Brereton RJ, Lister J. Catheters in spina bifida. *Z Kinderchir* 1982; **37**: 100–6.
8. Shapiro SR, Lebowitz R, Colodny AH. Fate of 90 children with ileal conduit urinary diversion a decade later; analysis of complications, pyelograpy, renal function and bacteriology. *J Urol* 1975; **114**: 289–95.
9. Cass AS, Luxenberg M, Gleich P, Johnson CF. A 22 year follow-up of ileal conduits in children with a neurogenic bladder. *J Urol* 1984; **132**: 529–31.
10. Rickwood AMK, Thomas DG. The upper renal tracts in adolescents and young adults with myelomeningocoele. *Z Kinderchir* 1984; **132**: 104–6.
11. Eckstein HB. Neuropathic bladder. In: Williams DI, ed. *Handbuch der Urologie: XV Supplement—Urology in Childhood*. Berlin: Springer-Verlag, 1974, 249–65.
12. Johnston JH, Shapiro SR, Thomas GG. Anti-reflux surgery in the congenital neuropathic bladder. *Br J Urol* 1976; **48**: 639–42.

13. Lapides J, Diokno AC, Silber SJ, Lowe BS. Clean intermittent self-catheterization in the treatment of urinary tract disease. *J Urol* 1972; **107**: 458–61.
14. Levit SB, Weiss RA. Vesicoureteral reflux—natural history, classification and reflux neuropathy. In: Kelalis PP, King LR, Belman AB, eds. *Clinical Paediatric Urology Vol 1*, 2nd ed. Philadelphia: WB Saunders, 1985, 365.
15. Gordon I. Renal diagnostic imaging. In: Williams DI, Johnston JH, eds. *Paediatric Urology*, 2nd ed. London: Butterworths, 1982, 11–26.
16. Politano VA, Leadbetter WF. An operative technique for the correction of vesicoureteral reflux. *J Urol* 1958; **79**: 932–41.
17. Urquhart-Hay D, McIlwaine J, Stephenson CBS. The use of a ureteric nipple alone for reflux prevention. *Br J Urol* 1977; **49**: 375–7.
18. Kaliciński ZH, Kansy J, Joszt W *et al.* Follow-up of surgical treatment of vesicoureteric reflux in 141 children. *Z Kinderchir* 1981; **32**: 157–69.
19. Ahmed A. Ureteral reimplantation by the transverse advancement technique. *J Urol* 1978; **119**: 547–50.
20. Williams DI. Vesico-ureteric reflux. In: Williams DI, ed. *Handbuch der Urologie: XV Supplement: Urology in Childhood.* Berlin: Springer-Verlag, 1974, 111–36.
21. Jeffs RD, Jonas P, Schillinger JF. Surgical correction of vesicoureteral reflux in children with neurogenic bladder. *J Urol* 1976; **115**: 449–51.
22. Mundy AR, Shah PJR, Borzyskowski M, Saxton HM. Sphincter behaviour in myelomeningocele. *Br J Urol* 1985; **57**: 647–51.
23. Van Gool JD, Kuijten RH, Donckerwolcke RA, Kramer PP. Detrusor-sphincter dyssynergia in children with myelomeningocele: A prospective study. *Z Kinderchir* 1982; **37**: 148–52.
24. Bauer SB. Management of neurogenic bladder dysfunction in children. *J Urol* 1984; **132**: 544–5.
25. Ransley PG. Vesico-ureteric reflux. In: Williams DI, Johnston JH, eds. *Paediatric Urology*. 2nd ed. London: Butterworths, 1982, 151–66.
26. Hirsch S, Carrion H, Gordon J, Politano V. Ureteroneocystostomy in the treatment of reflux in neurogenic bladders. *J Urol* 1978; **120**: 552–4.
27. Thomas G, Zachary RB, Lister J. 'Closed' external sphincterotomy for bladder outlet obstruction in myelomenigocele. *Br J Urol* 1973; **45**: 515–19.
28. Light JK, Scott FB. The artificial urinary sphincter in children. *Br J Urol* 1984; **56**: 54–7.
29. Warren MM, Kelalis PP, Stickler GB. Unilateral ureteroneocystostomy: the fate of the contralateral ureter. *J Urol* 1972; **107**: 466–8.
30. Purcell MH, Gregory JG. Intermittent catheterization: Evaluation of complete dryness and independence in children with myelomeningocele. *J Urol* 1984; **132**: 518–20.
31. Sullivan T, Purcell MM, Gregory JG. The management of vesicoureteric reflux in pediatric neurogenic bladder. *J Urol* 1981; **125**: 65–6.
32. Belloli L, Musi L, Campobasso P, Cattaneo A. Ureteral reimplantation in children with neurogenic bladder. *J Pediatr Surg* 1979; **14**: 119–27.
33. Bauer SB, Colodny AH, Retik AB. The management of vesicoureteral reflux in children with myelodysplasia. *J Urol* 1982; **128**: 102–5.
34. Hendren WH. Reoperative ureteral reimplantation: Management of the difficult case. *J Pediatr Surg* 1984; **15**: 770–86.
35. Kass EJ, Koff SA. The management of vesicoureteral reflux in children with neurogenic bladders. *Z Kinderchir* 1981; **34**: 379–83.
36. Puri P, Guiney EJ. Endoscopic correction of vesicoureteric reflux secondary to neuropathic bladder. *Br J Urol* 1986; **58**: 504–6.

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Effects of fundoplication on the antireflux mechanism

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Forty patients with a diagnosis of gastro-oesophageal reflux disease established by 24-h ambulatory pH monitoring were treated by a short 360° fundoplication. Results of postoperative evaluation at 6 months were compared with those from 50 normal volunteers. The amount of gastro-oesophageal reflux at pH monitoring decreased significantly and was less than the reflux in the normal subjects. The pressure and the intra-abdominal length of the distal oesophageal high-pressure zone increased significantly. The pressure was similar to that in the normal subjects while a significantly longer intra-abdominal part of the high-pressure zone was created. The clinical results of the operation were evaluated in 38 patients by an independent gastro-enterologist, and were considered to be excellent in 22 patients, good in 13, fair in 2 and poor in 1 patient. The antireflux procedure provided good control of the gastro-oesophageal reflux in our patients by restoring the major components of the antireflux mechanism.

Keywords: Gastro-oesophageal reflux disease, oesophagitis, hiatus hernia, fundoplication, oesophageal manometry, 24-h oesophageal pH monitoring

Surgical treatment of gastro-oesophageal reflux aims to restore the normal function of the gastric cardia. This includes providing a barrier against gastro-oesophageal reflux while still allowing the cardia to relax, and permitting normal swallowing and the ability to belch and vomit. The introduction of oesophageal function tests, including long-term pH monitoring, has provided the opportunity (objectively) to evaluate the competence of the antireflux barrier.

In the study described here we have determined the effects of fundoplication on the antireflux barrier by oesophageal manometry and 24-h ambulatory oesophageal pH monitoring, and have compared the findings with those made in normal subjects.

Patients and methods

The study group comprised 40 patients, 10 women and 30 men, with a mean age of 45 years (range 22–65 years) that were operated upon because of documented gastro-oesophageal reflux disease between 1982 and 1985. There were no patients with oesophageal strictures in the study, as the results of pH monitoring in these patients are unreliable. An additional five patients were operated upon during this period, but are not reported in this study as they refused to undergo the follow-up investigations. All patients underwent symptom evaluation, oesophagogastroduodenoscopy, oesophageal manometry and ambulatory 24-h oesophageal pH monitoring pre-operatively and 6 months postoperatively. At the postoperative review the patients were also interviewed by an independent gastro-enterologist, and their symptoms were assessed.

For comparison 50 volunteers were studied: these comprised 32 women and 18 men, with a mean age of 39 years (range 30–76 years) with no previous or current symptoms of gastrointestinal disease and normal findings on oesophagogastroduodenoscopy. They were recruited mainly from the hospital staff and their relatives, and were paid a minor sum for their participation. They underwent oesophageal manometry and ambulatory 24-h oesophageal pH monitoring.

Symptom evaluation

Before the oesophageal tests, symptoms were assessed. A scoring system modified after DeMeester[1] was used (*Table 1*). Postoperatively, an interview was conducted by a gastro-enterologist unaware of the results of the pre- and postoperative investigations. The patients were asked specifically about reflux symptoms as well as about their ability to vomit and belch and whether they experienced increased flatus after the operation; they were also asked if they had experienced any side-effects after the operation. The results of the operation were classified as excellent (completely recovered), good (major improvement with minor problems), fair (major improvement but still some significant symptoms or side-effects) or poor (minor or no improvement or a worsening).

Oesophagogastroduodenoscopy. This was performed with flexible endoscopes after topical anaesthesia of the pharynx. Oesophagitis was classified as grade 1 (erythema) or grade 2 (erosions or ulcerations in the distal oesophagus). Barrett's oesophagus was defined as a circumferential extension of gastric epithelium more than 3 cm up in the tubular oesophagus. A hiatus hernia was diagnosed when the distance between the impression of the diaphragmatic crus and the distal end of the tubular oesophagus exceeded 2 cm with the patient breathing quietly and with a non-inflated stomach.

Oesophageal manometry. This was performed using the stationary pull-through technique. A three-lumen water-perfused catheter with distal side holes at 5-cm intervals was used, connected to an Arndorfer hydrocapillary pump (Arndorfer Medical Specialities Inc., Wisconsin, USA). By manometry the pressure, length and intra-abdominal length of the distal oesophageal high-pressure zone were established, as well as the mean amplitude of the contraction waves in the distal 5 cm of the oesophagus.

Ambulatory 24-h oesophageal pH monitoring. This was performed using Synectics® ambulatory pH-monitoring equipment consisting of an antimony pH electrode, silver/silver chloride reference electrode and solid-state memory box. After calibration at pH 7 and 1, the pH electrode was introduced nasally and placed with the pH recording tip 5 cm above the oral margin of the distal oesophageal high-pressure zone previously located by manometry. The patients and the normal subjects were instructed to lead as normal a life as possible and

Table 1 *Grading of symptoms*

Symptom	Grading	
Heartburn	1	Occasional episodes
	2	Main reason for medical visit
	3	Continuous, interferes with daily activities
Acid regurgitation	1	Occasional, after big meals
	2	Predictable on position or straining
	3	Episodes of pulmonary aspiration
Dysphagia	1	Occasional, short duration
	2	Requires liquids to clear
	3	Episode of oesophageal obstruction requiring medical attention

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Table 2 *Symptoms reported before and after fundoplication*

		No. of patients with symptoms	
Symptom	Grade	Pre-operative	Postoperative
Heartburn	0	4	37
	1	7	3
	2	13	0
	3	16	0
Acid regurgitation	0	5	40
	1	17	0
	2	11	0
	3	7	0
Dysphagia	0	26	29
	1	0	7
	2	12	4
	3	2	0

Grade 0, refers to patients without symptoms

Table 3 *Endoscopic findings before and after fundoplication*

	No. of patients with symptoms	
Endoscopic findings*	Pre-operative	Postoperative
No oesophagitis	5	32
Oesophagitis†		
Grade 1	5	0
Grade 2	25	3
Barrett's oesophagus‡	4	2

* Endoscopy was performed in 39 patients pre-operatively and in 37 patients postoperatively. † Grade 1, erythema; grade 2, erosions or ulcerations in the distal oesophagus. ‡ Barrett's oesophagus, circumferential extension of gastric epithelium more than 3 cm up in the tubular oesophagus

to have normal meals, with the exception of acid food and beverages. After the monitoring the results were analysed on an IBM personal computer using a computer program (Esophogram, Gastrosoft). Reflux was expressed as the percentage of time when the oesophageal pH was below 4 and was analysed for the total monitoring time and for the supine and upright periods.

Surgical procedure

The operation was performed abdominally through a left transrectal or midline incision. The distal 5 cm of the oesophagus was mobilized and, if present, the hiatus hernia was reduced into the abdomen. The structures on the lesser gastric curve and the fundus and the short gastric vessels were not divided. The hiatus of the diaphragm was, if widened, narrowed by stitches in the crura dorsally to the oesophagus. A 36 french gastric tube was passed through the oesophagus into the fundus and the front wall of the fundus was passed dorsally and to the right side of the oesophagus. Three non-absorbable sutures were placed from the major curvature to the front wall of the oesophagus and to the gastric wall on the right side of the oesophagus. A 360° fundoplication 3 cm long was thus created, easily allowing at least one finger to be passed through the fundoplication. The fundoplication was not fixed to the diaphragm. The median operation time was 107·5 min (range 65–254 min); median peroperative blood loss was 300 ml (50–2600 ml) and median hospital stay was 6 days (3–16 days). Two patients underwent reoperation during the 6-month follow-up period, one because of a subphrenic abscess and one because of a small bowel obstruction 3 months postoperatively. There were four major complications: these comprised three splenectomies and the subphrenic abscess that was reoperated. There were two minor complications: one patient contracted pneumonia postoperatively and one a urinary tract infection. No patient died.

Statistical methods

The Mann–Whitney U test was used. A P value $<0\cdot05$ was considered to be statistically significant.

The investigation of the 50 normal volunteers was approved by the ethical research committee of the Lund University, 24 March, 1984.

Results

Symptoms

The effect of the operation on heartburn, acid regurgitation and dysphagia is shown in *Table 2*. Fourteen patients had dysphagia pre-operatively; it disappeared in nine of these after the operation. Of the 11 patients with postoperative dysphagia, 6 had developed it as a result of the operation while 2 were improved and 3 patients were unchanged. Thirty-eight of the patients were interviewed by a gastro-enterologist 6 months after the operation. The overall effect of the operation on the patients' symptoms was judged to be excellent in 22 cases, good in 13 cases, fair in 2 and poor in 1. Twenty-nine (76 per cent) patients declared, on direct questioning, that they could belch normally and 16 (42 per cent) experienced a disagreeable increase in flatus after the operation. None of the patients, however, had complaints of upper abdominal fullness and discomfort after eating. There were no significant differences in the pressure or the intra-abdominal length of the distal oesophageal high-pressure zone or amount of reflux, postoperatively, between patients with and without the ability to belch. Furthermore, there were no differences in these postoperative variables in patients with or without increased flatus. No patient had tried to vomit during the first 6 months after operation.

Endoscopic findings

Endoscopy was performed in 39 patients pre-operatively and in 37 patients postoperatively. The effect of the operation on the endoscopic findings are shown in *Table 3*. The endoscopic pathological changes were found to be healed in 29 patients, while 3 patients had persistent grade 2 oesophagitis and 2 had persistent Barrett's oesophagus. It is notable that Barrett's oesophagus had disappeared in two patients after the operation. All patients but one had a hiatus hernia pre-operatively; these were all found to be reduced at the time of the postoperative control examination.

Manometry (*Table 4*)

Pre-operatively, the median pressure in the distal oesophageal high-pressure zone was significantly lower in the patients than in the normal subjects ($P<0\cdot001$). Postoperatively, it had increased significantly ($P<0\cdot001$) and to a normal level. The median intra-abdominal length of the high-pressure zone was, similarly, shorter in the patients before the operation than in the controls ($P<0\cdot001$). The intra-abdominal length also increased significantly postoperatively ($P<0\cdot001$) and was then longer than the intra-abdominal length in the normal subjects ($P<0\cdot05$). The amplitude of the distal oesophageal contractions was not affected by the operation and did not differ significantly between patients and normal subjects.

pH monitoring

The effect of the fundoplication on ambulatory 24-h oesophageal pH monitoring is shown in *Figure 1*. The amount of reflux during the total monitoring time and the upright and

Table 4 *Results of oesophageal manometry*

Findings on manometry	No. of patients with symptoms		
	Pre-operative	Postoperative	Normals
HPZ pressure (mmHg)	6·4 (4·7–8·5)*	14 (12·7–16)	13·9 (9·3–17·3)
HPZ intra-abdominal length (cm)	1·5 (0·7–1·7)*	2·3 (2·0–3·0)**	2·0 (1·5–2·7)
Distal oesophageal contraction amplitudes (mmHg)	21 (12–28·5)	20 (15–28)	25 (20–27)

The results show the median and median interquartile range. HPZ, distal oesophageal high-pressure zone; *significantly different from postoperative and normal subjects; **significantly different from normal subjects

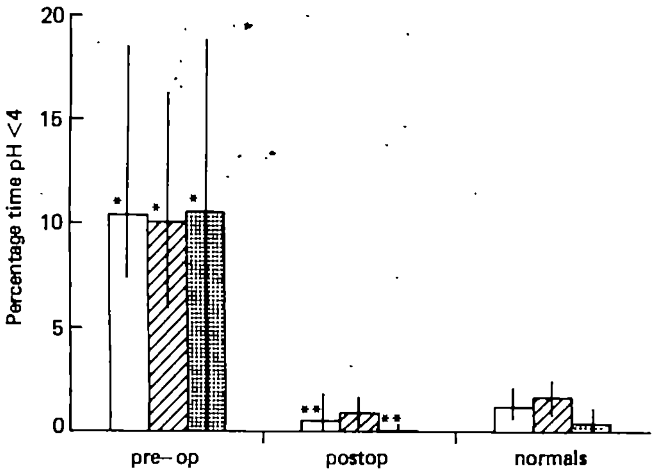

Figure 1 *Results of ambulatory 24-h oesophageal pH monitoring. Values are median and interquartile range. *Significantly different from postoperative and normals; **significantly different from normals;* ▦, *supine;* ■, *upright,* □, *total*

the supine periods was increased in the patients before the operation in relation to the normal subjects ($P<0{\cdot}001$). It decreased significantly after the operation ($P<0{\cdot}001$) and was less than the reflux of the normal subjects during the supine and total periods ($P<0{\cdot}001$), whereas the difference in reflux in the upright position between patients postoperatively and normal subjects did not reach statistical significance.

Discussion

In the study described here, a 360° fundoplication 3 cm in length provided good control of gastro-oesophageal reflux as measured by ambulatory pH monitoring and the patients' symptoms. The described technique, with no mobilization of the gastric fundus and the lesser curvature, in our hands reduced peroperative blood loss and operation time. The incidence of splenectomies in our study is similar to that reported by Polk[2]. Franklin *et al.*[3] have reported a higher incidence of splenectomies and also have shown that morbidity was significantly greater in the patients who underwent splenectomy. The single subphrenic abscess in our material occurred in one of the patients where splenectomy was performed, indicating that it is important to use an operative technique with as low a risk of splenic injury as possible.

The amount of reflux in the patients after the operation was less than that in the normal subjects, indicating that a supercompetent antireflux mechanism was created. The components of the antireflux mechanism that are affected by the fundoplication in our study are the pressure and the intra-abdominal length of the distal oesophageal high-pressure zone, while the oesophageal peristalsis is unaffected. Many studies have concluded that a normal pressure in the high-pressure zone is the major deterrent to reflux[4,5]. This pressure was low in our patients pre-operatively and returned to normal levels after the operation. The pressure values achieved are partly due to the transfer of gastric muscle tone around the distal oesophagus[6,7]. An adequate intra-abdominal length of the high-pressure zone is also essential for cardio-oesophageal competence[8]. The intra-abdominal length of the high-pressure zone was, in our study, greater in the operated patients than in the normal subjects. It has been shown experimentally[9] and clinically[10] that a repositioning of the cardia intra-abdominally without fundoplication is less effective in preventing reflux. Adequate intra-abdominal length is thus maintained by the fundoplication as it creates a conduit for transmission of intra-abdominal pressure changes around the intra-abdominal oesophagus.

The fundoplication performed thus prevents reflux caused by changes in intragastric and intra-abdominal pressure by directly transmitting the intragastric pressure to the high-pressure zone and by keeping the high-pressure zone intra-abdominal. It also prevents the shortening of the high-pressure zone that occurs with gastric dilatation[11]. There is evidence in our study that the high-pressure zone that we have created is supercompetent, because 24 per cent of the patients were unable to belch and 42 per cent suffered from increased flatus after the operation. Although the patients with increased flatus and inability to belch, in comparison with those without, did not have higher postoperative resting pressure or longer intra-abdominal length of the high-pressure zone, it is possible that the fundic wrap has become unnecessarily long in some patients. As the length of the intra-abdominal oesophagus was increased in our patients postoperatively, in relation to normal subjects, further shortening of the wrap may be warranted in the future. There is, on the other hand, experimental evidence[12] that the resting pressure achieved by a fundoplication is dependent on the length of the fundic wrap. Another explanation for the increased flatulence may be the habit of increased saliva swallowing, adopted by many patients with gastro-oesophageal reflux disease to reduce their heartburn. Six months without heartburn is perhaps too short a time to abandon this habit and the inability to belch adequately will increase the intestinal gas. DeMeester and Johnson[13] have reported a similar incidence of postoperative flatus. In their report a higher pressure was created by a 360 degree fundoplication but a shorter intra-abdominal length than in the present study. These differences may be due to differences in operative technique and emphasize the importance of performing thorough follow-up, including pH monitoring and manometry, after antireflux procedures in order to determine if refinements in technique are indicated.

The overall effects on the endoscopic findings were good in our population. The persisting oesophagitis in three patients may be due to streaks of columnar epithelium in the oesophagus that may persist without inflammation. Barrett's oesophagus disappeared after surgery in two of our patients. Skinner *et al.*[14] have reported the same phenomenon in two out of ten patients with Barrett's oesophagus after antireflux repair. They have interpreted this as a dislocation of the squamocolumnar junction following surgery and not necessarily as a result of squamous cell regeneration.

Fundoplication is a fairly successful operation for gastro-oesophageal reflux in patients carefully investigated pre-operatively, at least in terms of results after 6 months. The problems of difficulties in belching and increased flatus may perhaps be solved by shortening the fundoplication, as proposed by DeMeester[5]. Additional follow-up after 5 and 10 years will be needed to establish the final outcome of the operation.

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References

1. DeMeester TR, Wang C-I, Wernly JA *et al.* Technique, indications, and clinical use of 24 hour esophageal pH-monitoring. *J Thorac Cardiovasc Surg* 1980; **79**: 656–70.
2. Polk HC. Fundoplication for reflux esophagitis: misadventures with the operation of choice. *Ann Surg* 1976; **183**: 645–52.
3. Franklin RH, Iweze FI, Owen-Smith MS. Fundoplication for hiatus hernia. *Br J Surg* 1973; **60**: 65.
4. Haddad JK. Relation of gastro-esophageal reflux to yield sphincter pressures. *Gastroenterology* 1970; **58**: 175.
5. DeMeester TR. Gastro-esophageal reflux disease. In: Surgical treatment of digestive disease. Moody FG, ed. Chicago: Year Book Medical Publishers, 1986.
6. Bowes KL, Sarna SK. Effect of fundoplication on the lower esophageal sphincter. *Can J Surg* 1975; **18**: 328–33.
7. Condon RE, Kraus MA, Wollhein W. Cause of increase in lower esophageal sphincter pressure after fundoplication. *J Surg Res* 1976; **20**: 445–50.

8. DeMeester TR, Wernly JA, Bryant GH, Little AG, Skinner DB. Clinical and in vitro determinants of gastro-esophageal competence: a study of the principles of antireflux surgery. *Am J Surg* 1979; **137**: 39–46.
9. Leonardi HK, Lee ME, El-Kurd MF, Ellis FH. An experimental study of the effectiveness of various antireflux operations. *Ann Thorac Surg* 1977; **24**: 215–22.
10. DeMeester TR, Johnson LF, Kent AH. Evaluation of current operations for the prevention of gastro-esophageal reflux. *Ann Surg* 1974; **180**: 511–25.
11. Pettersson GB, Bombeck CT, Nyhus LM. The lower esophageal sphincter: mechanisms of opening and closure. *Surgery* 1980; **88**: 307–14.
12. Leonardi HK, Ellis FH, Cormack J, Gorrilla RN. Experimental fundoplication: comparison of results of different techniques. *Surgery* 1977; **82**: 514–20.
13. DeMeester TR, Johnson LF. Evaluation of the Nissen antireflux procedure by esophageal manometry and twenty-four hour pH monitoring. *Am J Surg* 1975; **129**: 94–100.
14. Skinner DB, Walther BC, Riddell RH, Schmidt H, Iascone C, DeMeester TR. Barrett's esophagus—comparison of benign and malignant cases. *Ann Surg* 1983; **198**: 554–66.

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Announcement

Reviews

The Editorial Board of *The British Journal of Surgery* continues to invite review articles on topics of interest to its readers. Any topic will be considered, but priority will be given to those addressing a major current problem. The author of each accepted review will receive an honorarium of £100. Potential authors seeking advice on the suitability of review topics are advised to contact: Professor D. C. Carter, University Department of Surgery, Royal Infirmary, Glasgow G31 2ER, UK.

Leading articles

The Editors invite submissions of signed leading articles to *The British Journal of Surgery*. These articles should be 600–1000 words in length, should address controversial topics of current interest and should be supported by key references. Submissions may be subjected to external review and assessment by the Editorial Board before acceptance. The Editors retain the right to alter style and shorten material for publication. An honorarium of £100 is payable on publication. Potential authors seeking advice on the suitability of topics are advised to contact: Professor D. C. Carter, University Department of Surgery, Royal Infirmary, Glasgow G31 2ER, UK.

Surgical workshops

The Editors invite the submission of articles describing technical innovations or modifications which may be useful in surgical practice. These articles should be less than 500 words long; they can be accompanied by no more than two figures but should not carry supporting references. Articles submitted to the Surgical Workshop series may be subjected to external review and assessment by the Editorial Board before acceptance.

Case reports

The British Journal of Surgery receives an increasing number of case reports each year. Space within the Journal remains at a premium and the rejection rate is likely to be high. Authors are advised to restrict such reports to a maximum of 500 words, to use no more than five references and to submit no more than one illustration.

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Left-sided subtotal oesophagectomy for carcinoma

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Oesophageal resection for carcinoma has been performed using a two-part left-sided approach with cervical anastomosis in 75 patients, all of whom have been followed up to death or for a minimum of 5 years. Operative mortality was 12 per cent, but long-term survival was 28 per cent for all squamous tumours and 12 per cent for all adenocarcinomas, irrespective of node status. It is suggested that this approach offers significant advantages.

Keywords: Oesophagus, carcinoma, resection

Over the past 20 years it has been established that resectable tumours of the oesophagus should be treated by subtotal oesophagectomy, irrespective of the level at which the tumour lies, in order to improve lymphatic clearance and reduce the incidence and consequence of anastomotic leaks[1,2]. The main technical problem for the surgeon is how this anatomical objective can be achieved. McKeown himself developed a three-part approach which involves a laparotomy, right thoracotomy and right neck incision[1]; this is a very lengthy procedure and an extensive abdominal dissection has to be done before it is possible to confirm that the tumour is resectable. Orringer, on the other hand, prefers a non-thoracic approach, with blunt extraction of the oesophagus and the tumour through a laparotomy and a neck incision[3].

The disadvantages of both these procedures can, however, be overcome by the use of a sequential two-part approach using a left thoracolaparotomy and left neck incision. Since 1976 this procedure has been performed on more than 300 patients in the Regional Thoracic Surgical Unit at East Birmingham Hospital, and the purpose of this paper is to describe the operative technique and results in the first 75 consecutive patients, all of whom have now been followed up to death or for a minimum period of 5 years.

Patients and methods

From August 1976 (representing the start of the first author's appointment) to December 1980 (to allow for 5-year follow-up on all patients), left-sided subtotal oesophagectomy was performed on 75 patients aged 38–76 years (mean 59·5) of whom 37 (50 per cent) were men. Tumours were located in the upper third of the oesophagus in 2 patients (3 per cent), in the middle third in 22 (29 per cent), in the lower third in 45 (60 per cent) and at the cardia in 6 (8 per cent). The histological type of tumour and node status, taken from the resected specimens, is shown in *Table 1*, together with the subsequent survival. At the time of operation resection was judged to be macroscopically complete in 60 patients (80 per cent) and definitely incomplete in 15 patients (20 per cent). An associated hiatus hernia was present radiologically in 12 patients (16 per cent), of whom 11 had an adenocarcinoma of the lower third or cardia (with a columnar lined oesophagus in 2 patients), and 1 patient had a squamous tumour of the lower third. During the period of this study resection was completed in 88 per cent of all cases that were explored, and of those resected 47 per cent had left-sided subtotal oesophagectomy, while 53 per cent had an intrathoracic anastomosis.

Pre-operative management. Investigations before operation were intended to assess the patient's fitness for the procedure and to determine whether there was spread of the tumour beyond the limits of surgical resection. Routine investigations included Hb, WCC, blood biochemistry, liver and lung function tests and ECG. Possible spread of the tumour was investigated by chest radiography, barium swallow, oesophagoscopy and biopsy, abdominal and liver ultrasound (or CT scan of the thorax and upper abdomen) in all cases, with bronchoscopy, indirect laryngoscopy, lymph node biopsy, cytology of effusions and other tests as indicated by symptoms or the findings on physical examination. Exploration with a view to resection was advised for all patients who were fit for operation and had no apparent distant disease. Pre-operative nutrition was maintained by dilatation at the time of oesophagoscopy and parenteral nutrition was not routinely employed. Before operation patients were required to stop smoking and received instruction in pulmonary physiotherapy.

Operation was performed under general anaesthesia, using a double lumen endotracheal tube for the thoracic part of the procedure (to allow the lung to be deflated) and a single lumen tube for the cervical part (to facilitate the neck anastomosis). In the latter half of the series a single dose of prophylactic antibiotic was given intravenously on induction of anaesthesia. The technique of operation is summarized as follows.

Part one—left thoracolaparotomy

With the patient in the right lateral position an oblique lateral incision is made starting in the left hypochondrium and continuing over the costal margin and along the line of the seventh rib to the angle of the ribs posteriorly. The superficial muscles are divided and the pleura opened along the upper border of the seventh rib using diathermy. The costal margin is cut cleanly with a scalpel and the diaphragm divided peripherally for approximately 15 cm close to its origin on the ribs and leaving the phrenic nerve undamaged. The peritoneum is opened in the line of the main incision from the centre of the abdominal edge of the diaphragmatic incision to the edge of the rectus sheath, giving a T-shaped exposure which provides very good access to the upper abdominal organs. In patients with a large associated hiatus hernia a left thoracotomy alone may suffice with the stomach being mobilized through the oesophageal hiatus without opening the diaphragm or dividing the costal margin, which is particularly beneficial for frail, elderly patients with borderline respiratory function.

Assuming the growth is resectable the stomach is first examined to confirm that it is free from tumour or other disease and suitable for taking up to the neck. The oesophagus and tumour are then mobilized from the oesophageal hiatus upwards, into the root of the neck. The oesophagus is freed from behind the aortic arch by blunt dissection in the plane between the oesophageal muscle and the adjacent connective tissue thereby avoiding damage to the recurrent laryngeal nerve. A finger is passed behind the aortic arch so that its tip appears beneath the superior mediastinal pleura above the arch and this pleura is then incised and a tape passed around the oesophagus above the aortic arch to facilitate mobilization of the upper oesophagus into the root of the neck.

The oesophagogastric junction and stomach are then mobilized fully, dividing the short gastric vessels and the left and right gastric arteries. The right gastro-epiploic artery and vein are meticulously preserved as the viability of the whole of the stomach depends on these vessels. Splenectomy is not routinely performed.

When the stomach is fully mobilized two strong transfixion sutures are placed through the oesophagus just below the aortic arch (either above or below the tumour according to its location) and the oesophagus divided transversely between them. The lower oesophagus is then brought down through the hiatus and the lower oesophagus and stomach lifted out of the wound. The fat and glands along the lesser curve and left gastric artery are then excised and the oesophagogastric junction cleaned. A Payr's crushing clamp is placed tangentially below

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Table 1 *Histology, node status and survival in 75 patients having left-sided subtotal oesophagectomy*

	n	Postoperative deaths	Alive at 1 year	Alive at 5 years
Squamous				
Node negative	21	—	19	9 (43%)
Node positive	18	4	6	2 (11%)
Adenocarcinoma				
Node negative	10	1	8	3 (30%)
Node positive	23	4	7	1 (4%)
Anaplastic				
Node negative	1	—	1	—
Node positive	2	—	1	—
Totals	75	9 (12%)	42 (56%)	15 (20%)

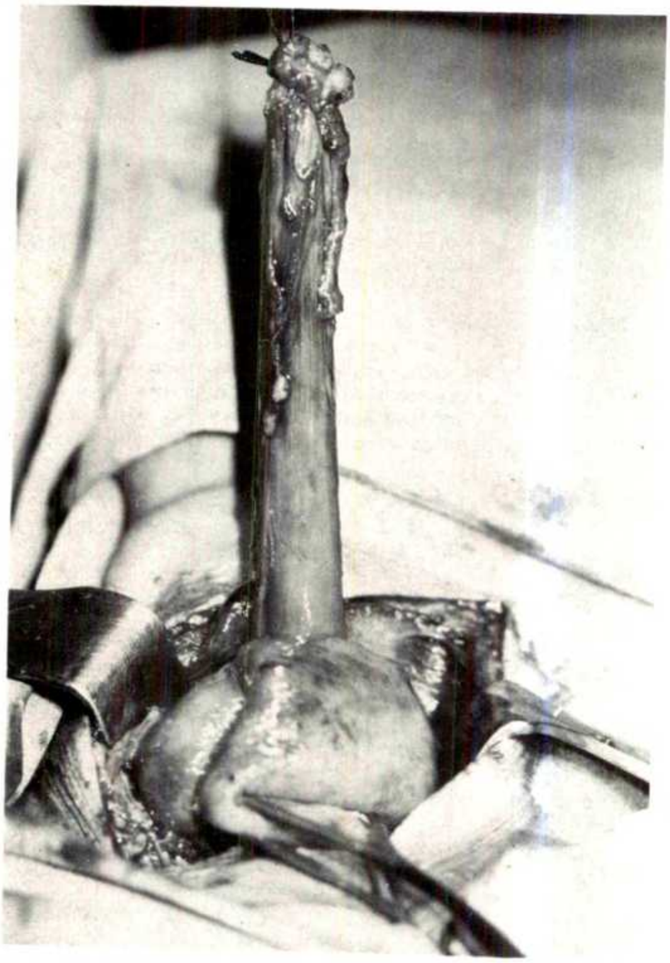

Figure 1 *Proximal oesophagus and fundus of the stomach delivered through the cervical incision before oesophagogastric anastomosis*

the oesophagogastric junction and the lower oesophagus excised. This line of section is then closed and invaginated in two layers with continuous Dexon (Davis and Geck, UK) and silk. To facilitate gastric drainage a longitudinal posterior pyloromyotomy is performed without opening the gastroduodenal mucosa.

The stomach is then taken up through the oesophagus hiatus and the stump of the oesophagus sutured securely to the fundus of the stomach, at the point which will later be used for the anastomosis, and passed medially to the aortic arch and positioned so that a 'bubble' of fundus lies in the apex of the left chest. The diaphragm, chest and abdomen are then closed in layers using Dexon, with a size 32 Argyle intercostal drain through a separate stab incision.

Part two—left neck incision

With the patient supine and redraped an oblique incision 10 cm long is made along the anterior border of the left sternomastoid muscle. The omohyoid muscle is divided, together with the middle thyroid vein and the inferior thyroid artery if these are in the way of the exposure. The carotid and jugular vessels are retracted laterally and the trachea medially to expose the already mobilized oesophagus. Because the cervical oesophagus has already been mobilized from within the chest, no attempt is made to identify or dissect out the left recurrent laryngeal nerve. The oesophagus and fundus of the stomach are delivered through the wound and disconnected, the stomach being held with Duval forceps to prevent it slipping back into the chest (*Figure 1*). A stoma is then cut in the fundus of the stomach and end-to-end anastomosis performed between the oesophagus and the fundus, using one layer of continuous 36G monofilament stainless steel wire. The fundus of the stomach is then returned to the chest so that the completed anastomosis lies comfortably in the lower part of the incision and the neck is closed in layers with Dexon without drainage.

Postoperative management is kept as simple as possible. Nasogastric tubes and artificial ventilation are not used routinely and intravenous fluids are limited to 2 litres of 5 per cent dextrose per 24 h, plus blood volume replacement as necessary. Oral fluids are commenced on the second day with 30 ml of water hourly, followed by 60 ml on the third day, when the chest drain is removed, and 90 ml on the fourth day, when the intravenous infusion is discontinued. Feeding then progresses gradually to semi-solid and solid diets and a routine barium swallow is obtained before discharge which is usually on the 10th postoperative day.

Results

Early and late survival in the 75 patients in relation to histology and node status is shown in *Table 1*. Death within 30 days of operation occurred in nine patients (12 per cent). In the 15 patients with incomplete removal of the growth there were five deaths (33 per cent), due to respiratory failure in two, anastomotic leaks in two and irreversible shock in one; by contrast, in the 60 patients with complete removal of the growth there were only four deaths (7 per cent), due to respiratory failure in two, anastomotic leak in one and pulmonary embolism in one.

Non-fatal complications occurred in 25 patients (33 per cent), consisting of wound infection in 13 (mostly in early patients who did not receive antibiotics), air leak in two, localized anastomotic leak in three, respiratory difficulties in two, gastric outlet obstruction in two and left ventricular failure, deep vein thrombosis and jaundice in one each. No patient developed a chylothorax or had clinical recurrent nerve damage and the remaining 41 patients (55 per cent) made an uncomplicated recovery. Fifteen patients (20 per cent) were alive and free of recurrence 5 years after resection, with a 28 per cent 5-year survival for all squamous tumours, irrespective of node status, and 12 per cent 5-year survival for all adenocarcinomas. Following discharge from hospital one patient required drainage of a late right basal empyema, two required dilatations for anastomotic strictures and six (8 per cent) required dilatation for recurrence of the tumour, from 6 to 27 months after resection.

Discussion

The perfect operation for carcinoma of the oesophagus has yet to be devised. Each of the present options has its own specific advantages and disadvantages and the choice depends largely on personal preference and which factors are thought to be most relevant to the success of the procedure. The merits of subtotal oesophagectomy for all tumours which originate within the oesophagus have been well documented by McKeown[2], but the operation which he introduced is both time consuming and 'back to front,' as the abdominal part has to be performed before resectability of the tumour is established.

The two-part left-sided approach, as described here, overcomes these difficulties. Moreover, if the resectability of the tumour is in doubt, then the initial incision can be confined to the anterior abdominal part of the exposure or a limited thoracotomy, according to the location of the tumour or the areas of possible spread. If the tumour is not resectable then the wound is closed and the patient treated by endoscopic dilatation or intubation, without further surgical interference. If the growth is resectable then operation proceeds through the full incision and is complete within 3–4 h which allows two (or even on one occasion three) resections to be performed on the same day. An additional advantage of the left-sided approach is that the right mediastinal pleura is usually left intact, so that the stomach remains confined between it and the aortic arch and there is therefore much less tendency for it to prolapse into the right chest and interfere with pulmonary function.

The left-sided thoracic approach also has significant advantages over the transhiatal resection which has been advocated by Orringer[3]. Tumours at any level can be removed under direct vision with optimal clearance and without the risk of recurrent laryngeal nerve damage or inaccessible bleeding. Orringer favours the abdominal approach partly because it is supposed to cause less complications, but the complication rate of 48 per cent which he has recently reported[4] is no better than the 45 per cent rate reported here.

The 12 per cent postoperative mortality rate in this series is comparable with other recent British series (using predominantly intrathoracic anastomoses)[5,6], but the 5-year survival rates of 28 per cent for all squamous tumours and 12 per cent for all adenocarcinomas are noticeably better. It is difficult to determine whether this is due to different case selection from other series, as they do not generally relate survival to histology and node status, or to the proportion of incompletely resected cases which was 20 per cent in this series. In general, however, we feel that the good long-term results tend to support McKeown's contention that removal of the whole thoracic oesophagus with cervical anastomosis (i.e. subtotal oesophagectomy), under direct vision, offers the best prospects of long-term survival for the patient with resectable carcinoma of the oesophagus.

From 1976 to 1979 left-sided subtotal oesophagectomy was used in only 47 per cent of oesophageal resections performed in this Unit, but the improved results soon became apparent and from 1980 to the present time this procedure has become the operation of choice and has been used in 86 per cent of all oesophageal resections for carcinoma. The procedure is contraindicated only if the tumour is situated exactly at the aortic arch, for which the standard three-part right-sided approach is used, or if the fundus of the stomach is involved and there is insufficient stomach to reach to the neck, when a conventional oesophagogastrectomy with intrathoracic subaortic anastomosis is preferred.

References

1. McKeown KC. Trends in oesophageal resection for carcinoma. *Ann R Coll Surg Engl* 1972; **51**: 213–38.
2. McKeown KC. The surgical treatment of carcinoma of the oesophagus: a review of the results in 478 cases. *J R Coll Surg Edinb* 1985; **30**: 1–14.
3. Orringer MB, Sloan HS. Esophagectomy without thoracotomy. *J Thorac Cardiovasc Surg* 1978; **76**: 643–54.
4. Goldfaden D, Orringer MB, Appelman HCV, Kalish R. Adenocarcinoma of the distal esophagus and gastric cardia: comparison of results of transhiatal esophagectomy and thoracoabdominal esophagogastrectomy. *J Thorac Cardiovasc Surg* 1986; **91**: 242–7.
5. Dark JF, Mousalli H, Vaughan R. Surgical treatment of carcinoma of the oesophagus. *Thorax* 1981; **36**: 891–5.
6. Watson A. A study of the quality and duration of survival following resection, endoscopic intubation and surgical intubation in oesophageal carcinoma. *Br J Surg* 1982; **69**: 585–8.

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The 66th Meeting of the Surgical Research Society took place on 9 and 10 July 1987 at the University of Leeds. The meeting was organized by the University Department of Surgery, Leeds General Infirmary, and Professor P. R. F. Bell was in the Chair. A Symposium entitled 'Basic science and surgical aspects of the ileocaecal region, anus and pelvic ileal reservoirs' preceded the free paper sessions. One hundred and four papers were read, and the Patey Prize was awarded to Dr P. C. Sedman for his presentation entitled 'Augmentation of lymphokine activated killer cell activity in patients with gastrointestinal cancer'.

Discrimination is not impaired by excision of the anal transition zone after restorative proctocolectomy

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Anal sensation has been assessed using a constant current stimulator in 21 patients after restorative proctocolectomy (15 J pouch, 6 W pouch). The anal transition zone (ATZ) has been excised in 15 patients but preserved in 6. Results were compared with 14 age- and sex-matched patients with ulcerative colitis (UC) and 14 controls. Median threshold values in the lower, mid and upper zones of the anal canal in pouch patients were: 6·8 mA, >15·0 mA and >15·0 mA respectively compared with 3·9 mA ($P<0.01$), 5·7 mA ($P<0.01$) and 11·4 mA ($P<0.01$) in UC and 3·5 mA ($P<0.01$), 4·2 mA ($P<0.01$) and 11·4 mA ($P<0.01$) in controls. The mid and upper zone threshold anal sensation was significantly lower when the ATZ had not been removed and except in the lower zone did not differ from UC or controls (median threshold sensations when ATZ was preserved were: lower zone, 5·8 mA; mid zone, 5·5 mA; upper zone, 7·5 mA). Paired studies in eight patients showed that excision of the ATZ was associated with a significant impairment in anal sensation (mid zone: 5·7 versus *>15·0 mA,* $P<0.05$*; upper zone: 7·5* versus *>15·0 mA,* $P<0.05$*) whereas no change in anal sensation was recorded when the ATZ was preserved. Despite these physiological changes, no clinical benefit could be identified in patients in whom the ATZ was preserved. Discrimination was normal in all except one patient. The incidence of soiling, nocturnal incontinence and failure to defer defaecation for more than 1 h was recorded in 3/15 patients (20 per cent) whose ATZ had been removed, compared with 1/6 patients (17 per cent) in whom the ATZ had been preserved. We conclude that excision of the ATZ does not eliminate the ability to discriminate and does not increase the risk of impaired continence after ileo-pouch anal anastomosis.*

Keywords: Restorative proctocolectomy, ileo-anal pouch, sensation, discrimination, anal transition zone

Duthie and Gairns recognized an area of anal epithelium of variable length above the anal valves which is associated with organized nerve endings. This area, known as the anal transition zone (ATZ), is thought to have an important role in the ability to discriminate gas from liquid or solid stool. This zone is also thought to be responsible in the afferent pathway for the recto-anal inhibitory reflex[2,3]. Nevertheless some doubt has been cast on this theory since Read and Read[4] reported no objective impairment of continence following application of local anaesthetics to the anal canal. It is possible that afferent sensory fibres may, in fact, be located in the external sphincter and the puborectalis muscles[5]. Despite this, Roe and others[6] have recently indicated that anal sensation is impaired among patients with idiopathic faecal incontinence, suggesting with others that there is both a motor and sensory deficit in the territory supplied by the pudendal nerve[7]. Impaired temperature sensation has also been demonstrated in these patients[8].

The operation of restorative proctocolectomy aims to remove all the diseased mucosa in ulcerative colitis (UC). Traditionally, the colon and most of the rectum is excised and the remaining mucosa stripped to the level of the anal valves[9–12]. In some clinical series there has been a high incidence of soiling and impaired discrimination after restorative proctocolectomy[13–16]. For these reasons it has been suggested that the ATZ should be preserved during restorative proctocolectomy[17], particularly as the ATZ is rarely severely affected by colitis[18].

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Therefore, we have studied sensory function correlated with clinical outcome in 21 patients following restorative proctocolectomy, 6 of whom have had their ATZ preserved. We have compared these results with 14 age- and sex-matched patients with ulcerative colitis (UC) and with 14 normal controls.

Patients and methods

Twenty-one patients who had had a successful restorative proctocolectomy were studied (*Table 1*): 15 had a duplicated (J) pouch reconstruction and 6 had a quadruple (W) pouch. In six patients the ATZ was preserved (3 J and 3 W pouches). Results were compared with 14 age- and sex-matched pre-operative patients with ulcerative colitis and 14 age- and sex-matched controls. Paired studies have been undertaken before operation and 6 months after closure of the ileostomy in eight patients (ATZ preserved in two). A clinical assessment of bowel function included frequency of defaecation during the day and night, evidence of any soiling 6 months after operation, episodes of true incontinence, urgency, ability to defer defaecation for more than 1 h, the wearing of pads and the ability to discriminate gas from semi-solid stool.

Anal sensation was measured in the high-pressure zone of the anal canal. As this zone is variable, all patients had their resting anal canal pressures assessed by a closed water-filled balloon probe using static measurements over 6 cm or using a station pull-through technique[19]. Threshold sensation was measured in three zones within the high-pressure segment of the anal canal (low, mid and upper zones) with a constant-current stimulator using a modification of the device described by Roe and colleagues[6]. Our instrument employed a monopolar electrode to avoid the production of two responses at the test site and to locate more precisely the area being measured. An increased pulse width and a wider probe were also used to minimize variation in the contact area. Using a pulse width of 0·1 ms our instrument recorded threshold sensation over a range 0–15·0 mA.

Measurement obtained on different days in 12 patients who had undergone restorative proctocolectomy showed that the test was reproducible (coefficient of variation $r=0{\cdot}976$: ($P<0{\cdot}001$)). Intra-observer variation was tested in 10 subjects, who had a variety of anorectal disorders, by three observers and this was also reproducible ($r=0{\cdot}957$, $P<0{\cdot}001$).

Table 1 *Groups studied*

Group	Median age	Male	Female
Controls	23 (17–64)	7	7
Ulcerative colitis (UC)	24 (18–63)	7	7
Restorative proctocolectomy	21 (18–62)	9	12
J pouch	15 (18–45)	6	9 (ATZ preserved 3)
W pouch	6 (18–62)	3	3 (ATZ preserved 3)

Results

Threshold sensation in patients after proctocolectomy was significantly impaired in all three zones of the anal canal, compared with patients with UC and controls (*Table 2*). However, threshold anal sensation in the mid and upper zone did not differ from UC patients or controls if the ATZ had been preserved (*Figure 1*). There was a small difference in threshold

Table 2 *Median range threshold anal sensation (mA)*

	Anal zones		
	Lower	Mid	Upper
Controls	3·5 (1·5–7·2)	4·2 (3·0–6·4)	7·0 (3·9–12·7)
UC	3·9 (2·4–8·7)	5·7 (2·7–8·0)	11·4 (5·7–> 15·0)
Restorative proctocolectomy	6·8 (2·9–> 15·0)**	> 15·0 (5·5–> 15·0)**	> 15·0 (5·5–> 15·0)**
ATZ preserved	5·8 (3·8–8·5)*	5·5 (4·6–7·0)	7·5 (6·0–> 15·0)
ATZ excised	9·7 (2·9–> 15·0)***	> 15·0 (8·2–> 15·0)***	> 15·0 (All > 15·0)***

ATZ, anal transition zone; UC, ulcerative colitis.
* $P<0{\cdot}05$ compared with control and UC
** $P<0{\cdot}01$ compared with control and UC
*** $P<0{\cdot}001$ compared with control and UC

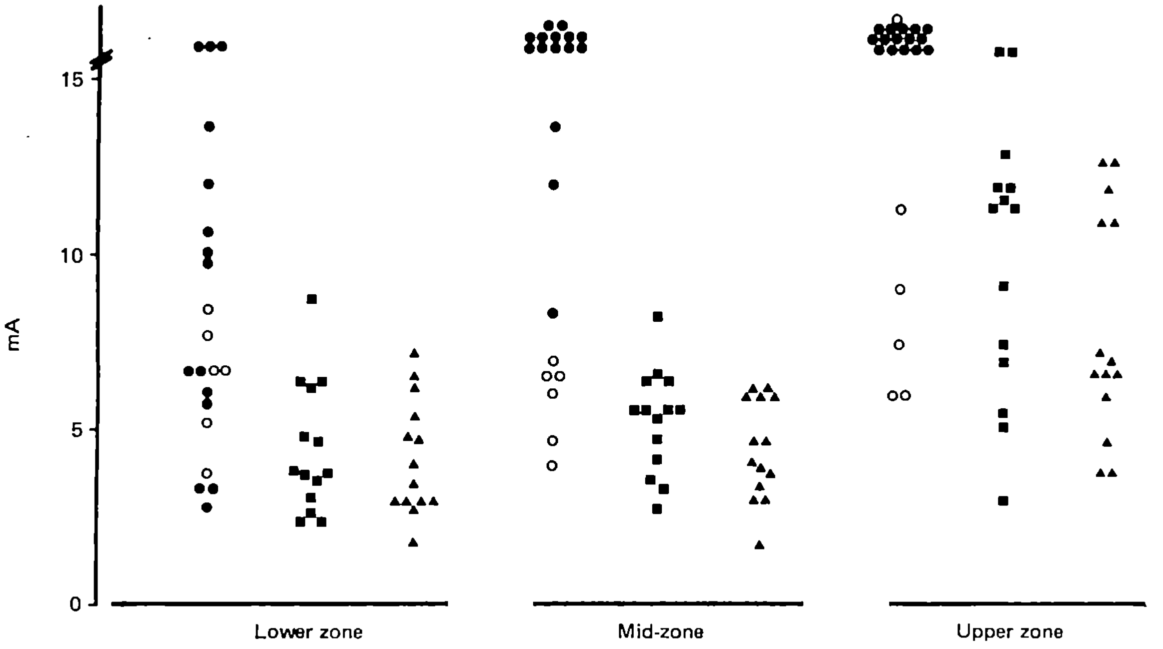

Figure 1 *Threshold anal sensation in the three anal zones after restorative proctocolectomy, compared with ulcerative colitis* (■) *and controls* (▲) (● *= anal transition zone removed,* ○ *= anal transition zone preserved*)

sensation in the low zone, even when the ATZ was preserved, compared with controls ($P<0{\cdot}05$).

Paired studies in eight patients before and 6 months after closure of the loop ileostomy after restorative proctocolectomy have shown a significant impairment in threshold sensation in the mid ($P<0{\cdot}05$) and upper zones ($P<0{\cdot}05$) where the ATZ had been excised but not in any of the zones in the two patients in whom the sensory zone had been preserved (*Table 3*, *Figure 2*).

Despite these objective changes in anal sensation, no functional differences could be detected, irrespective of whether the ATZ had been excised or preserved (*Table 4*). Frequency of diarrhoea was identical. Soiling, nocturnal incontinence or inability to defer defaecation for an hour, occurred in 3/15 patients after excision of the ATZ (20 per cent) compared with 1/6 patients in whom the ATZ was preserved (17 per cent). Although the use of pads and urgency were more common in the former group, there were other factors which in our view were responsible for these poor results. Five patients were classified as having imperfect results. All of these patients have been studied physiologically using the saline infusion test, pouch compliance and simultaneous pouch, ileal and anal pressures at rest, during defaecation and after maximal pelvic floor contraction. One of the patients had no demonstrable physiological abnormality while all of the remainder had a small irritable J pouch with poor compliance and early leakage of saline. All of these patients had had postoperative pelvic sepsis. In only one of these patients was there objective evidence of impaired anal sensation as well as a failure to discriminate gas from liquid stool. Indeed, discrimination was observed in all except one patient, despite excision of the ATZ.

Table 3 *Threshold anal sensation in lower, mid and upper zone: paired studies (mA) before and 6 months after closure of the loop ileostomy in 8 patients*

	Before			After		
	Lower	Mid	Upper	Lower	Mid	Upper
ATZ preserved	3·8	5·4	7·0	3·8	7·0	11·4
	6·8	6·8	7·5	6·8	6·8	7·5
				n.s.	n.s.	n.s.
ATZ excised	3·5	8·9	>15·0	10·0	>15·0	>15·0
	8·7	5·7	5·7	6·0	>15·0	>15·0
	3·7	5·7	9·2	6·8	>15·0	>15·0
	4·8	3·6	11·4	>15·0	>15·0	>15·0
	6·2	6·7	7·5	7·9	>15·0	>15·0
	6·5	6·5	7·0	6·8	>15·0	>15·0
				n.s.	$P<0{\cdot}05$	$P<0{\cdot}05$

ATZ, anal transition zone.

Discussion

Assessment of anal sensation is reproducible from day to day and intra-observer variation is small. Objective loss of anal sensation correlates well with the extent of the anal mucosectomy. Like others, we have demonstrated objective impairment of anal sensation in incontinent patients and in some patients with chronic constipation (references 6 and 8 and K. Yoshioka, F. Heyen, M.C. Winslet, M.R.B. Keighley, unpublished results).

Despite objective loss of anal sensation after excision of the ATZ, loss of discrimination by these patients was

Table 4 *Functional results in 21 patients after restorative proctocolectomy*

Result	15 ATZ excised	6 ATZ preserved
Bowel frequency: day/night	5/1	6/1
Soiling	3	1
Pads (only at night)	4	1
Nocturnal incontinence	3	1
Urgency	3	0
Inability to defer defaecation for more than 1 h	3	1
Failure to discriminate gas from semi-solid	1	0

ATZ, anal transition zone.

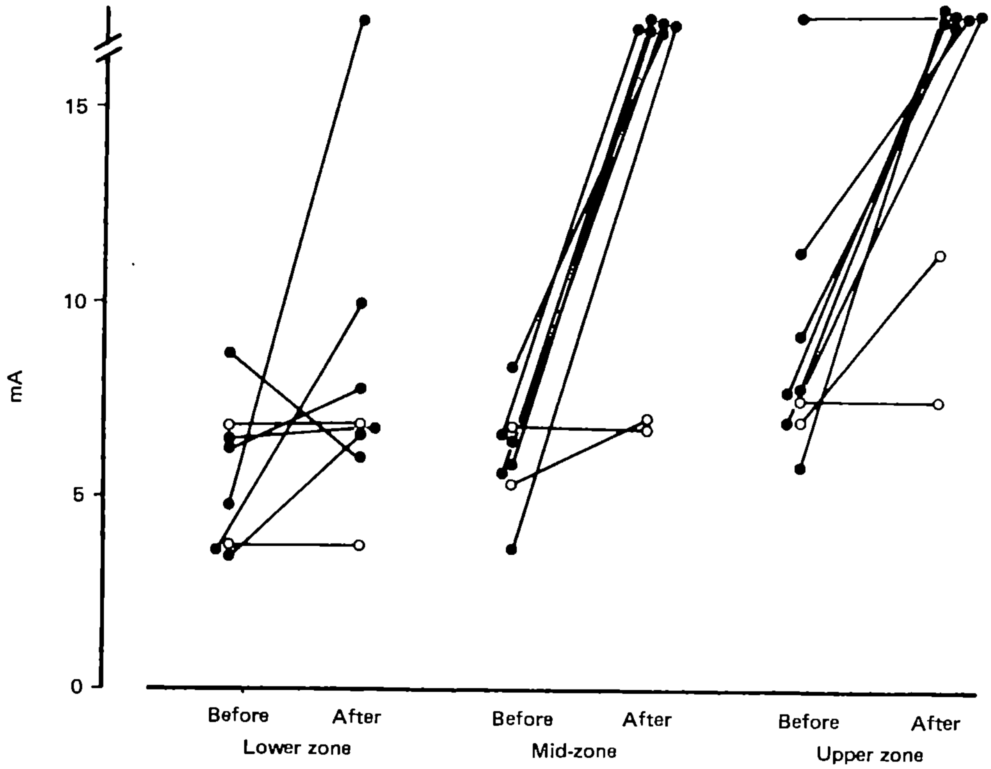

Figure 2 *Changes in threshold and sensation: paired observations in eight patients before and after restorative proctocolectomy (● = anal transition zone removed, ○ = anal transition zone preserved)*

observed in only one subject. All others had normal discrimination despite an anaesthetic upper anal canal. It is possible that the lower anal canal may provide sufficient sensory awareness to provide this function[20]. It is also possible that discrimination may be preserved if this is mediated by awareness of pressure changes in the pouch, as was proposed in the intact rectum by Goligher[21]. Certainly, our experience of patients after restorative proctocolectomy indicates that pouch sensation is quite acute with threshold volumes of between 20 and 60 ml and a feeling of constant sensation of between 40 and 100 ml. These parameters do not differ markedly from those of the intact rectum[22]. Afferent impulses induced by pressure changes may be due to stretch receptors in the external sphincter and puborectalis[23]. Following colo-anal anastomosis patients are usually aware of distension in the neorectum. Unlike Lane and Parks[24], we were unable to demonstrate preservation of the inhibitory reflex after colo-anal or ileo-anal pouch construction (reference 25 and K. Yoshioka, F. Heyen, M. C. Winslet, M. R. B. Keighley, unpublished results). In our experience the inhibitory reflex is not retained even after preserving the ATZ.

The other defects in defaecation after pouch anal anastomosis in this series, such as urgency, failure to defer defaecation, incontinence, soiling and frequency could almost certainly be explained by other physiological factors. The majority of these patients either had impaired resting anal pressure, possibly due to excessive intra-anal retraction[26], or had non-compliant duplicated pouches associated with previous pelvic sepsis. These factors have been reported to be associated with impaired pouch function[27,28].

We are in no doubt from these data that preservation of the ATZ retains anal sensation but that discrimination is preserved despite excision of this zone of sensory anal epithelium. Indeed, preservation of the ATZ *per se* does not seem to be associated with superior functional results.

References

1. Duthie HL, Gairns FW. Sensory nerve endings and sensation in the anal region of man. *Br J Surg* 1960; **47**: 585–95.
2. Duthie HL, Bennett RC. The relation of the sensation in the anal canal to the functional anal sphincter: a possible factor in anal continence. *Gut* 1963; **4**: 179–82.
3. Bartolo DCC, Read NW, Jarrat JA, Read MG, Donnelly TC, Johnson AG. Differences in anal sphincter function and clinical presentation in patients with pelvic floor descent. *Gastroenterology* 1983; **85**: 68–75.
4. Read MG, Read NW. Role of anorectal sensation in preserving continence. *Gut* 1982; **23**: 345–7.
5. Scharli AF, Keisewetter WB. Defaecation and continence: some new concepts. *Dis Colon Rectum* 1970; **13**: 81–107.
6. Roe AM, Bartolo DCC, Mortensen NJMcC. New method for assessment of anal sensation in various anorectal disorders. *Br J Surg* 1986; **73**: 310–2.
7. Rogers J, Henry MM, Misiewicz JJ. Combined sensory and motor deficit in primary neuropathic faecal incontinence. *Gut* (in press).
8. Miller R, Bartolo DCC, Mortensen NJMcC. Anorectal temperature sensation: a comparison of normal and incontinent patients. *Br J Surg* 1986; **74**: 511.
9. Parks AG, Nicholls RJ. Proctocolectomy without ileostomy for ulcerative colitis. *Br Med J* 1978; **2**: 85–8.
10. Johnston D, Williams NS, Neal DE, Axon ATR. The value of preserving the anal sphincter in operations for ulcerative colitis and polyposis: a review of 22 mucosal proctectomies. *Br J Surg* 1981; **68**: 874–8.
11. Rothenberger DA, Buls JG, Nivatvongs S, Goldberg SM. The Parks S ileal pouch and anal anastomosis after colectomy and mucosal proctectomy. *Am J Surg* 1985; **149**: 390–4.
12. Taylor BM, Beart RW Jr, Dozois RR, Kelly KA, Phillips SF. Straight ileoanal anastomosis v ileal pouch-anal anastomosis after colectomy and mucosal proctectomy. *Arch Surg* 1983; **118**: 696–701.
13. Cohen Z, McLeod RS, Stern H, Grant D, Nordgren S. The pelvic pouch and ileoanal anastomosis procedure. Surgical technique and initial results. *Am J Surg* 1985; **150**: 601–7.
14. Williams NS, Johnston D. Mucosal proctectomy and ileo-anal anastomosis. In: Taylor I, ed. *Progress in Surgery, Vol 1.* Edinburgh, London: Churchill Livingstone, 1985: 95–113.
15. Metcalf AM, Dozois RR, Kelly KA, Beart RW Jr, Wolfe BG. Ileal 'J' pouch-anal anastomosis. Clinical outcome. *Ann Surg* 1985; **202**: 735–9.
16. Nasymth DG, Williams NS, Johnston D. Comparison of the function of triplicated and duplicated pelvic ileal reservoirs after mucosal proctectomy and ileoanal anastomosis for ulcerative colitis and adenomatous polyposis. *Br J Surg* 1986; **73**: 361–6.
17. Primrose JN, Holdsworth PJ, Nasmyth DG, Womack N, Neal DE, Johnston D. Intact anal sphincter with end-to-end ileo-anal anastomosis for ulcerative colitis: comparison with mucosal proctectomy and pull-through anastomosis. *Br J Surg* 1987; **74**: 539.
18. Deasy P, Quirke P, Dixon M, Lagopoulos M. Johnston D. The surgical importance of the anal transitional zone in ulcerative colitis. *Br J Surg* 1987; **74**: 533.
19. Shouler P, Keighley MRB. Changes in colorectal function in severe idiopathic chronic constipation. *Gastroenterology* 1986; **90**: 414–20.
20. Gould RP. Sensory innervation of the anal canal. *Nature* 1960; **187**: 337–8.
21. Goligher JC. The functional results after sphincter saving resections of the rectum. *Ann R Coll Surg Engl* 1951; **8**: 421–39.
22. Farthing MJG, Lennard-Jones JE. Sensibility of the rectum to distension and the anorectal distension reflex in ulcerative colitis. *Gut* 1978; **19**: 64–9.
23. Henry MM, Swash M. *Coloproctology and the Pelvic Floor. Pathophysiology and Management*. London: Butterworth, 1985.
24. Lane RHS, Parks AG. Function of the anal sphincters following colo-anal anastomosis. *Br J Surg* 1977; **64**: 596–9.
25. Keighley MRB, Matheson D. Functional results of rectal excision and endo-anal anastomosis. *Br J Surg* 1980; **67**: 757–61.
26. Keighley MRB. Abdominal mucosectomy reduces the incidence of soiling and sphincter damage after restorative proctocolectomy and J pouch. *Dis Colon Rectum* 1987; **30**: 386–90.
27. Nasmyth DG, Johnson D, Godwin PGR, Dixon MF, Smith A, Williams NS. Factors influencing bowel function after ileal pouch-anal anastomosis. *Br J Surg* 1986; **73**: 469–73.
28. Nicholls RJ, Pezim ME. Restorative proctocolectomy with ileal reservoir for ulcerative colitis and familial adenomatous polyposis: a comparison of three reservoir designs. *Br J Surg* 1985; **72**: 470–4.

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Factor X-activating activity in patients with colorectal carcinoma

The ability of malignant tissue from 50 patients with colorectal carcinoma to activate blood coagulation factor X directly was compared with samples of adjacent, macroscopically normal colonic mucosa from the same patients, and tissue from four patients with non-malignant bowel disease. The resected tissue was homogenized and incubated with purified factor X and calcium ions. The subsequent generation of activated factor X was measured spectrophotometrically with a chromogenic substrate. Results were expressed as absorbance units, and as the ratio of tumour and normal activities. Factor X-activating activity (FXAA) was present in all normal and malignant tissues tested. FXAA was significantly greater (P < *0·001) in the tumour homogenates than in the uninvolved tissue. The tumour: normal ratio was significantly* (> *1·2) elevated in 38 patients (76 per cent). FXAA was not correlated with the degree of differentiation of the tumour, the Dukes' classification of the disease or the exact site of the tumour. There was no difference between the FXAA content of non-involved tissue from the colorectal cancer group and colonic mucosa from patients with non-malignant bowel disease. It is concluded that colorectal carcinomas contain significantly more FXAA than adjacent, non-malignant colonic mucosa from the same subject, but there is no direct evidence for a relationship between procoagulant levels and the extent of malignancy in these patients.*

Keywords: Blood coagulation, factor X, colorectal cancer

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The clinical relationship of cancer and thrombosis[1], and the histological association of fibrin and tumour deposits[2], have been recognized for more than a century. There is increased activation of the blood coagulation system in patients with various forms of malignant disease[3], and a significantly higher frequency of occult malignancy in patients with deep vein thrombosis[4]. The possibility that tumour cells secrete a procoagulant activity which might account for these findings was suggested by the observation that malignant tissues shorten the clotting times of recalcified plasma significantly more than most normal tissues[5]. The presence of tissue factor activity in human malignant tissue is now well recognized[6–9], although this factor VII-dependent pathway is not the only mechanism by which tumours can activate blood coagulation. A glycoprotein found in mucus extracts[10] activates factor X directly, and Gordon and co-workers[11] later described another type of factor VII-independent, factor X-activating activity in malignant tumours. This activity, termed cancer procoagulant A (CPA), has since been reported in a number of experimental[12,13] and human[14,15] malignancies. The identification of CPA was of particular interest for two main reasons: first, it appeared that CPA was specific for malignant differentiation, as normal tissue contained only tissue factor[11,14]; secondly, studies in animal models have shown that dietary deficiency of vitamin K[16] and oral anticoagulants[17] interfere with tumour spread and reduce the cellular levels of the cancer procoagulant[18,19], providing a biochemical basis for the use of vitamin K antagonists in cancer treatment[20].

Cancer procoagulant has previously been identified in a limited number of human colon carcinomas[11,14] and a human colon carcinoma cell line[21]. However, these studies provided no information on the relationship of the procoagulant activity to the degree of malignant differentiation or stage of the disease. The purpose of the study described here was, therefore, to compare the ability of these tumours to activate factor X, using a specific chromogenic assay, with adjacent non-involved colonic mucosa, and to correlate the result with Dukes' classification and the degree of differentiation of the tumours.

Patients and methods

Sample collection

Fifty patients undergoing surgery for resection of colorectal tumours, and four patients who were subsequently found to have non-malignant bowel disease (three patients with diverticulitis and one with 'constipation'), were studied. The resected tissue was collected before addition of formalin or any other solution. Samples of tumour were then cut from areas of viable malignant tissue, avoiding the necrotic tumour centre. Portions of macroscopically uninvolved tissue were then stripped from the proximal end of the bowel samples, but clear of the resected margins.

Tissue homogenization

The tissue samples were weighed and added to a tenfold (w/v) volume of calcium-free balanced salt solution. The tissues were finely minced with crossed scalpel blades before being mechanically homogenized for 60 s. Homogenates were then centrifuged at 10 000 rev/min for 1 min and the clear supernatant used to assay procoagulant activity.

Procoagulant assay

Factor X-activating activity (FXAA) was determined in a specific chromogenic assay adapted from the method of Colucci *et al.*[22]. Normal or tumour tissue extract (0·1 ml) was incubated with 0·1 ml calcium chloride (0·025 M), 0·1 ml (0·2 units) purified bovine factor X (Sigma Chemical Company) and 0·2 ml buffer (0·05 M Tris-HCl, pH 7·8) for 2 h at 37°C. Generation of factor Xa was then stopped by addition of 0·5 ml assay buffer containing 7·5 mM EDTA. Chromogenic substrate (0·2 ml 3 mM; CBS 31.39, Diagnostic Stago Ltd) was added, and the incubation continued for a further 30 min. This reaction was then terminated by addition of 0·3 ml 40 per cent trichloroacetic acid and the precipitated protein was removed by centrifugation at 10 000 rev/min for 1 min. The supernatant was decanted, and neutralized by addition of 0·16 ml 5 M NaOH. The optical density of the solution was then read at 405 nm in a Pye–Unicam SP500 spectrophotometer against a blank containing

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Table 1 *Factor X-activating activity in homogenates of colonic mucosa from four patients with non-malignant bowel disease, fifty with colorectal tumours and corresponding adjacent, non-involved mucosa. Results are expressed as absorbance values and as the ratio of tumour and normal absorbance values*

Results	*n*	Median	Interquartile range
Absorbance (405 nm)			
Non-malignant mucosa	4	0·43	0·37–0·50
Adjacent, non-malignant mucosa	50	0·34	0·14–0·49
Tumour tissue	50	0·64	0·26–0·77
Ratio (tumour/normal)			
All patients	50	1·56	1·22–2·08
Male patients	26	1·75	1·25–2·00
Female patients	24	1·46	1·14–2·08

Table 2 *Statistical analysis of factor X-activating activity ratios in 50 patients with colorectal adenocarcinoma classified according to Dukes*

Dukes' classification	*n*	Median	Interquartile range
A	6	1·62	1·25–2·20
B	24	1·52	1·14–2·00
C	20	1·62	1·25–2·14

assay buffer in place of factor X. To correct for non-calcium-dependent protease activity, the absorbance of a tube containing no added calcium ions was subtracted from the total activity. Procoagulant activities were expressed in optical density units and as the ratio of absorbance values of the tumour and corresponding normal mucosa.

Statistics

As the procoagulant activity data did not conform to a normal distribution, the median value and interquartile range was calculated for each group of patients. Differences between groups were assessed with the Mann–Whitney *U* test.

Results

Statistical analysis of the FXAA results is shown in *Table 1*. The median FXAA level in tumour tissue was significantly higher ($P<0{\cdot}001$) than in adjacent, non-involved colonic mucosa. In individual patients, the ratio of tumour activity to that of corresponding uninvolved tissue was taken to be significantly elevated when it exceeded 1·2. An elevated ratio, indicating significantly higher tumour-associated FXAA, was obtained in 38/50 (76 per cent) of patients. There was no significant difference in FXAA ratios between male and female patients.

There were no differences in median FXAA ratios between patients with colon adenocarcinoma classified according to Dukes' stage (*Table 2*), the degree of malignant differentiation (*Table 3*) or the tumour site (*Table 4*).

Samples of colonic mucosa were also obtained from four patients with non-malignant pathology. The median FXAA level in this group was not significantly different from the non-involved tissue resected from patients with colorectal carcinoma.

Discussion

There is an increasing amount of clinical and experimental support for a close relationship between blood coagulation and the spread of malignant disease. The possibility that tumour cells might secrete procoagulant activities has been studied by numerous workers, but the precise relationship of such products to the course of the malignant process remains unclear. The presence of a protease with specific FXAA in a variety of malignant tissues has been extensively studied[11–15,21–25]. This procoagulant is primarily characterized by its ability to activate factor X in the absence of factor VII, thus distinguishing it from tissue factor which requires factor VII to initiate coagulation.

The present study has demonstrated the presence of a procoagulant, capable of directly activating factor X, in resected tumour tissue from patients with colorectal carcinoma in significantly greater amounts than in normal, uninvolved colonic mucosa. Although FXAA was also detected in all normal tissue samples tested, malignant tissue contained significantly higher quantities in 76 per cent of the patients studied. These findings are broadly comparable with the data of Gordon *et al.*[14], who described higher levels of FXAA in colorectal adenocarcinoma tissue compared with non-involved colonic mucosa in four out of six patients studied.

The FXAA demonstrated in normal and malignant bowel tissue in the present study awaits detailed biochemical characterization, but its independence of factor VII is confirmed by the type of assay system employed. Most previous studies of tumour-related procoagulant activity have relied on the ability of the tissue extracts to accelerate the clotting time of recalcified citrated plasma. In such experiments, differentiation of tissue factor activity and FXAA has been achieved by the ability of the latter to potentiate clotting of plasma deficient in factor VII. In the present study, the ability of the tissue samples to activate factor X was specifically assessed in a purified system in which factor X was the only clotting factor present. Activation of factor X is reflected by the generation of yellow *para*-nitroanaline from a factor Xa-sensitive chromogenic substrate and assessed spectrophotometrically. Compared with clotting methods for assessing procoagulant activity, the technique used here has the advantages of absolute specificity, sensitivity and freedom from observer errors which may influence clotting tests.

Previous studies, which included a limited number of colorectal tumours[14], have suggested that malignant tissue contains a specific factor X activator, whereas the procoagulant associated with normal tissue is primarily tissue factor. This contention is not supported by the present investigation which has shown the presence of specific FXAA in both normal and malignant bowel tissue. Although macroscopically uninvolved colonic mucosa in colorectal cancer patients may not be truly 'normal', the FXAA content was not significantly different from mucosa resected from patients with non-malignant bowel disease. This suggests that colorectal malignancy is associated with a *quantitative* change in a normal type of procoagulant activity, and not by a *qualitative* change associated with malignant differentiation.

Table 3 *Statistical analysis of factor X-activating activity ratios in 46 patients with colorectal adenocarcinoma classified according to the degree of malignant differentiation. This information was not available for the remaining four patients*

Degree of differentiation	*n*	Median	Interquartile range
Good	13	1·83	1·14–2·21
Moderate	27	1·47	1·25–2·17
Poor	6	1·61	1·56–2·14

Table 4 *Statistical analysis of factor X-activating activity ratios in 50 patients with colorectal adenocarcinoma classified according to the site of the tumour*

Tumour site	*n*	Median	Interquartile range
Caecum	11	1·54	1·22–1·79
Ascending colon	7	2·08	2·00–2·39
Transverse colon	4	2·35	2·17–2·52
Sigmoid colon	10	1·66	1·45–1·91
Rectum	18	1·89	1·25–2·00

Studies in experimental animals have suggested that the procoagulant content of a particular tumour may be related to its metastatic potential[25,26]. The demonstration of FXAA apparently identical to that described in malignant tissue in extracts of amnion-chorion[27] raises the possibility that the procoagulant is an oncofetal protein that is expressed in undifferentiated fetal cells and in dedifferentiated malignant cells. In the study described here, however, there was no correlation between the FXAA content and the invasiveness of the tumour as measured by Dukes' stage, or the degree of malignant differentiation.

The possibility that FXAA might represent a new type of γ-carboxylated protein dependent on vitamin K for its synthesis has been suggested[19]. This hypothesis is particularly attractive in view of the effect of oral anticoagulants on the growth and spread of various experimental tumours[17] and reduction in cellular procoagulant activity[18]. Whether the procoagulant described in the present study is vitamin K dependent is not yet known. However, preliminary experiments (J. L. Francis and K. El-Baruni, unpublished results) show that the procoagulant activity is dependent on calcium ions and binds to aluminium hydroxide and barium salts—properties that are compatible with the presence of γ-carboxyglutamic acid residues[28].

In conclusion, tumours from patients with colorectal carcinoma contain significantly higher levels of a procoagulant capable of directly activating coagulation factor X. The procoagulant levels did not appear to be related to the Dukes' classification or the degree of malignant differentiation. Whether these findings have implications for the use of oral anticoagulants in the treatment of human colorectal cancer awaits experimental support.

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References

1. Trousseau A. Phlegmasia alba dolens. In: *Clinique Medicale de l'Hotel de Paris*. London: Ballière, 1865: Vol. 3, 654–6.
2. Billroth T. *Lectures on Surgical Pathology and Therapeutics*, translated from the 8th edition. London: New Sydenham Society, 1878.
3. Rickles FR, Edwards RL. Activation of blood coagulation in cancer: Trousseau's syndrome revisited. *Blood* 1983; **62**: 14–31.
4. Goldberg RJ, Seneff M, Gore JM *et al.* Occult malignant neoplasm in patients with deep venous thrombosis. *Ann Intern Med* 1987; **147**: 251–3.
5. O'Meara RAQ. Coagulative properties of cancers. *Irish Med J* 1958; **394**: 474–9.
6. Sakuragawa N, Takahashi K, Hoshiyama M *et al.* The extract from the tissue of gastric cancer as procoagulant in disseminated intravascular coagulation syndrome. *Thromb Res* 1977; **10**: 457–63.
7. Szczepanski, M, Lucer C, Zawadzki J, Tolloczko T. Procoagulant and fibrinolytic activities of gastric and colorectal cancer. *Int J Cancer* 1982; **30**: 329–33.
8. Mussoni L, Conforti G, Gambacorti-Passerini C *et al.* Procoagulant and fibrinolytic activity of human ovarian carcinoma cells in culture. *Eur J Cancer Clin Oncol* 1986; **22**: 373–80.
9. Zacharski LR, Memolia VA, Rousseau SM. Coagulation–cancer interaction in situ in renal cell carcinoma. *Blood* 1986; **68**: 394–9.
10. Pineo GF, Regoeczi E, Hatton MWC, Brain MC. The activation of coagulation by extracts of mucus: a possible pathway of intravascular coagulation accompanying adenocarcinomas. *J Lab Clin Med* 1973; **82**: 255–66.
11. Gordon SG, Franks JJ, Lewis B. Cancer procoagulant A: a factor X activating procoagulant from malignant tissue. *Thromb Res* 1975; **6**: 127–37.
12. Curatolo L, Colucci M, Cambini AL *et al.* Evidence that cells from experimental tumours can activate factor X. *Br J Cancer* 1979; **40**: 228–33.
13. Hilgard P, Whur P. Factor X-activating activity from Lewis Lung carcinoma. *Br J Cancer* 1980; **41**: 642–3.
14. Gordon SG, Franks JJ, Lewis B. Comparison of procoagulant activities in extracts of normal and malignant human tissue. *J Natl Cancer Inst* 1979; **62**: 773–6.
15. Donati MB, Gambacorti-Passerini C, Casali B *et al.* Cancer procoagulant in human tumour cells: Evidence from melanoma patients. *Cancer Res* 1986; **46**: 6471–4.
16. Hilgard P. Experimental vitamin K deficiency and spontaneous metastases. *Br J Cancer* 1977; **35**: 891–2.
17. Hilgard P, Schulte H, Wetzig G, Schmitt G, Schmidt CG. Oral anticoagulation in the treatment of a spontaneously metastasising murine tumour (3LL). *Br J Cancer* 1977; **35**: 78–85.
18. Poggi A, Colucci M, Delaini F, Semeraro N, Donati MB. Reduced procoagulant activity of Lewis Lung carcinoma cells from mice treated with warfarin. *Eur J Cancer* 1980; **16**: 1641–2.
19. Delaini F, Colucci M, De Bellis Vitti G *et al.* Cancer cell procoagulant: a novel vitamin K-dependent activity. *Thromb Res* 1981; **24**: 263–6.
20. Donati MB, Semeraro N. Cancer procoagulants and their pharmacological modification. *Haemostasis* 1984; **14**: 422–9.
21. Gordon SG, Gilbert LC, Lewis BJ. Analysis of procoagulant activity of intact cells from tissue culture. *Thromb Res* 1982; **26**: 379–87.
22. Colluci M, Curatolo L, Donati MB, Semeraro N. Cancer cell procoagulant activity: evaluation by an amidolytic assay. *Thromb Res* 1980; **18**: 589–95.
23. Gordon SG, Lewis BJ. Comparison of procoagulant activity in tissue culture medium from normal and transformed fibroblasts. *Cancer Res* 1979; **38**: 2467–72.
24. Gordon SG, Cross BA. A factor X-activating cysteine protease from malignant tissue. *J Clin Invest* 1981; **67**: 1665–71.
25. Gilbert LC, Gordon SG. Relationship between cellular procoagulant activity and metastatic capacity of B16 mouse melanoma variants. *Cancer Res* 1983; **43**: 536–40.
26. Donati MB, Semeraro N, Gordon SG. Relationship between procoagulant activity and metastatic capacity of tumour cells. In: Honn KV, Sloane BF, eds. *Hemostatic Mechanisms and Metastasis*. Boston: Martinus Nijhoff, 1984: 82–95.
27. Gordon SG, Hasiba U, Cross BA, Poole MA, Falanga A. Cysteine proteinase procoagulant from amnion-chorion. *Blood* 1985; **66**: 1261–5.
28. Suttie JW. Synthesis and secretion of vitamin K-dependent clotting factors. In: Glaumann H, Peters T, Redman C, eds. *Plasma Protein Secretion by the Liver*. London: Academic Press, 1983: 375–403.

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Randomized trial comparing anorectal myectomy and controlled anal dilatation for outlet obstruction

A randomized controlled study has compared anorectal myectomy (n = *13*) *with anal dilatation* (n = *10*) *using Park's anal retractor for patients with constipation. No patient was able to defaecate spontaneously more than three times a week before the operation. Of the 13 patients, 7 were able to defaecate spontaneously more than three times a week after anorectal myectomy, compared with none after anal dilatation* ($P<0{\cdot}05$). *None of the patients in either group became incontinent. There was a significant fall of anal canal pressure after anorectal myectomy at rest, during maximum pelvic floor contraction, and attempted defaecation: median, 100* (*range, 21–200*) *to 43* (*20–133*) *cm*H_2O, $P<0{\cdot}01$; *140* (*79–238*) *to 86* (*43–153*) *cm*H_2O, $P<0{\cdot}01$; *127* (*79–208*) *to 86* (*29–167*) *cm*H_2O, $P<0{\cdot}005$. *A significant improvement in rectal emptying occurred after anorectal myectomy* (*median, 0 per cent/min* (*range, 0–83*) *to 50* (*0–100*) *per cent/min*, $P<0{\cdot}025$). *On the other hand, anal dilatation was not associated with any significant change in rectal emptying or anal pressure. Pre-operative anal pressures during attempted defaecation in patients who achieved a good result after anorectal myectomy were significantly higher than those that did not* (*median, 136* (*range, 120–208*) versus *114* (*79–129*) *cm*H_2O, $P<0{\cdot}025$). *Patients having a good result after anorectal myectomy had a significantly shorter history of constipation* (*median, 4* (*range, 2–14*) versus *38* (*4–72*) *years*, $P<0{\cdot}01$) *and normal colonic transit* (*median, 100* (*range, 4–100*) versus *10* (*0–90*) *years*, $P<0{\cdot}05$) *compared with those who had no benefit after operation.*

Keywords: Anorectal myectomy, anal dilatation, chronic constipation, anal canal pressure

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Idiopathic chronic constipation can be classified into two broad functional groups: 'outlet obstruction' and 'colonic inertia'[1]. Outlet obstruction is characterized by a failure to defaecate because the pelvic floor does not relax during attempted defaecation. This condition can be identified by electromyographic evidence of increased activity of the puborectalis muscle during defaecation, or by proctographic evidence of failure to expel rectal contents during defaecation[2,3]. Colonic inertia is a condition where constipation is due to slow transit in the colon and can be assessed by radio-opaque transit markers and colonic motility studies[3,4].

Anorectal myectomy has been performed for patients with constipation, principally as a method of excluding short segment Hirschsprung's disease. We have been interested in the therapeutic effect of anorectal myectomy since improved function has been reported in children with Hirschsprung's disease having anorectal myectomy[5–7].

Encouraging results after anorectal myectomy have also been reported in adult patients with constipation. Our previous assessment has suggested that the therapeutic effect of the operation is merely to reduce resting anal canal pressure[8]. However, it has not been clear whether the reduction in resting anal canal pressure is achieved by excising a strip of the internal sphincter and rectal smooth muscle or simply by the anal dilatation resulting from the use of a Park's anal retractor during the procedure. Indeed, manual anal dilatation has been proposed as a method of treatment for constipation and achieves a significant and sustained fall in resting anal pressure[9,10]. Therefore, a randomized trial was designed to compare anorectal myectomy with controlled anal dilatation using a Park's retractor both to evaluate functional results and to study physiological changes before and after the operation.

Patients and methods

Twenty-three patients who were referred for investigation of constipation from May 1986 to March 1987 have entered a randomized trial. Randomization was by computer generated numbers where 13 patients underwent anorectal myectomy and 10 had a controlled anal dilatation using an intra-anal retractor. Anorectal myectomy was performed under general anaesthesia as previously described[8]. An intra-anal retractor was inserted into the anal canal and opened so as to separate the lateral edges of the anus by 5 cm. The mucosa was dissected off the internal sphincter over a distance of 10 cm. A third retractor blade was inserted under the mucosa exposing the internal sphincter and rectal circular muscle. The intersphincteric plane was developed posteriorly over a distance of 10 cm. A long haemostat was placed on the internal sphincter and rectal muscle and a 10 cm long, 0·5 cm wide segment of smooth muscle was excised. After haemostasis, the mucosal defect was closed with cat-gut and a sponge tamponade inserted in the rectum. A 5 cm wide anal dilatation was carried out using an intra-anal retractor for 20 min under general anaesthesia while three full-thickness biopsies were taken from the anterior wall of the anorectum and the rectal defects closed by continuous cat-gut suture. We deliberately avoided taking biopsies from the posterior wall of the anorectum because if the anal dilatation was unsuccessful an anorectal myectomy could then be performed on the posterior wall without the fibrosis from previous biopsies hindering a satisfactory anatomical dissection.

Clinical assessment was carried out before and 3 months after the operation. Manometric assessment, proctograms, colonic transit studies and electromyography were also carried out at the same time. These physiological studies were not carried out after the operation in

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Table 1 *Comparison of groups*

	Total	Anorectal myectomy	Anal dilatation
Number of patients	23	13	10
Male	1	1	0
Female	22	12	10
Median age (years)	35 (21–72)	38 (26–72)	35 (21–44)
Median history of constipation (years)	20 (2–72)	6 (2–72)	22 (2–43)
Hirschsprung's disease	4	2	2
Median bowel habit (/month)			
Pre-operative	2	2	2
Postoperative	11	18	2

Ranges are given in parentheses

two patients because one patient having anorectal myectomy became pregnant after the operation and another having anal dilatation refused to have repeat physiological examination afterwards.

Anal canal and sigmoid pressures were measured simultaneously at 2, 4 and 26 cm from the anal verge after digital examination with the patient in the seated position on a specially designed chair. Manometry was performed using a water perfused 4-channel catheter with side-openings connected to a pressure transducer (Lectromed) and multichannel recorder (MultiTrace 4, Lectromed). The catheter was introduced into the sigmoid colon with the patient in left lateral position. In five patients lateral plain X-rays of the pelvis were taken to confirm the position of the catheter. The catheter was fixed to the left buttock by tape. Pressures were measured at rest, during maximum pelvic floor contraction and attempted defaecation. Rectal compliance and the recto-anal inhibitory reflex were assessed using a rectal balloon attached to the 4-channel catheter and positioned in the rectal ampulla just above the levator ani. The balloon was also connected through the catheter to the pressure transducer and pen recorder. Balloon pressure responses to incremental increases in intrarectal volume were measured over the range 0–400 ml of air. Rectal compliance was calculated by dividing the increase in balloon volume by that of the pressure inside the balloon. Reduction of more than 10 per cent of the resting anal pressure was recorded as an intact recto-anal inhibitory reflex.

Rectal sensation was assessed using the same rectal balloon. Three parameters of sensation were recorded according to the criteria of Farthing and Lennard-Jones[11]: threshold volume, volume associated with constant rectal sensation and volume, below 400 ml, at which pain became intolerable (maximum tolerable volume). In many of the constipated patients a volume of 400 ml caused no apparent discomfort, but further volumes were not introduced for fear of bursting the balloon.

The saline infusion test was designed to test liquid continence. A 4-channel polyvinyl catheter (external diameter, 5 mm) with side openings at 2, 4, 19 and 26 cm from the anal verge was inserted digitally into the sigmoid. The catheter was connected to pressure transducers and a multichannel recorder so that the pressures at 2, 4 and 26 cm from the anal verge could be recorded while isotonic saline was being infused into the sigmoid through a 19 cm side hole in the catheter. The patient was seated on a special chair during the saline infusion test. A total of 1500 ml of isotonic saline (37°C) was infused at a rate of 50 ml/min by means of a peristaltic pump (H.R. Flow Inducer, Watson-Marlow Limited) and the subject was instructed to retain the saline for as long as possible without leakage. A commode was placed under the seat to collect any fluid that leaked from the anus. The volume infused at the time of the inital leak and the total volume retained were recorded (total volume retained = volume infused (1500 ml) − volume leaked).

Colonic transit was assessed before operation while the patient was eating a normal diet and taking no laxatives. Fifty radio-opaque pellets were taken by mouth and a plain X-ray of the abdomen was obtained 5 days later. Transit was recorded as the percentage of radio-opaque markers passed within 5 days.

Electromyography of the pelvic floor was recorded using a concentric needle electrode. Electrical activity was recorded at rest, during maximum pelvic floor contraction and after attempted defaecation. Electrical activity in normal subjects was always reduced during attempted defaecation. If there was greater electrical activity during defaecation than at rest, this phenomena was considered to be a feature of outlet obstruction.

Anorectal angles were measured from radiographs taken during defaecating proctograms with the patient seated on a lavatory pan using 100 ml (120 g) of Baritop mixed with cellulose to achieve a consistency similar to that of faeces. The angle between the anal canal and the axis of the rectum was assessed at rest, during maximum pelvic floor contraction and attempted defaecation using an image intensifier linked to a video screen. The long axis of the rectum was obtained by drawing a line through the anorectal junction and the 'centroid' of the rectum. The centroid was defined as that point which could divide a lateral projection of the rectum into two equal areas. The centroid was determined using a mathematical formulation programmed to analyse lateral radiographs using a BBC microcomputer.

Rectal emptying was also assessed during proctography by asking the patient to evacuate as much of the introduced contrast material (120 g) as possible during one min. The result was expressed as a percentage of the infused material.

Statistical analysis of the physiological data was made using the Mann–Whitney U test. The Fisher's exact test was used to compare the groups clinically.

Results

A comparison between the two randomized groups is shown in *Table 1*. There was only one man in the study. There were two patients who had histological evidence of short segment Hirchsprung's disease in each group.

Natural bowel habit (no laxative, bowel stimulants or suppositories) was compared before and 3 months after operation. No patient was able to defaecate spontaneously more than three times a week before operation in both groups, whereas bowel frequency significantly increased after anorectal myectomy. However, there was no significant difference in frequency of defaecation after anal dilatation. The result of anorectal myectomy was classified into two groups: those patients who were able to defaecate spontaneously more than three times a week after the operation were classified as having had a 'good result', and the remainder as having had a 'poor result' (*Table 2*). Seven patients (54 per cent) achieved a good result and 6 (46 per cent) had a poor result. History of constipation in the patients having a good result was significantly shorter than the remainder ($P<0{\cdot}01$). Both patients who had histological evidence of Hirschsprung's disease achieved a good result.

Anal canal pressures at 2 cm from the anal verge were compared before and 3 months after operation (*Figure 1*) but the two patients who did not undergo postoperative physiological studies were excluded from statistical analysis. Anal pressures at rest, during maximum pelvic floor contraction and attempted defaecation significantly decreased after anorectal myectomy, whereas no significant changes were observed after anal dilatation. Anal pressures amongst patients who achieved a good result fell significantly at rest, during maximum pelvic floor contraction and attempted defaecation, whereas there was no significant change after the operation in the 'poor result' group (*Figure 2*). Pre-operative anal canal pressures in patients who achieved a good result tended to be higher than in those who did not, and this was statistically different in the pressures recorded during attempted defaecation (*Figure 3*). Anal pressures at 4 cm from the anal verge and sigmoid pressures at

Table 2 *Results of anorectal myectomy*

	Total	Good result	Poor result
Number of patients (%)	13	7 (54)	6 (46)
Median bowel habit (/month)			
Pre-operative	2	2	1
Postoperative	18	32	1
Median history of constipation (years)*	6 (2–72)	4 (2–24)	38 (4–72)
Hirschsprung's disease	2	2	0

* Ranges are given in parentheses

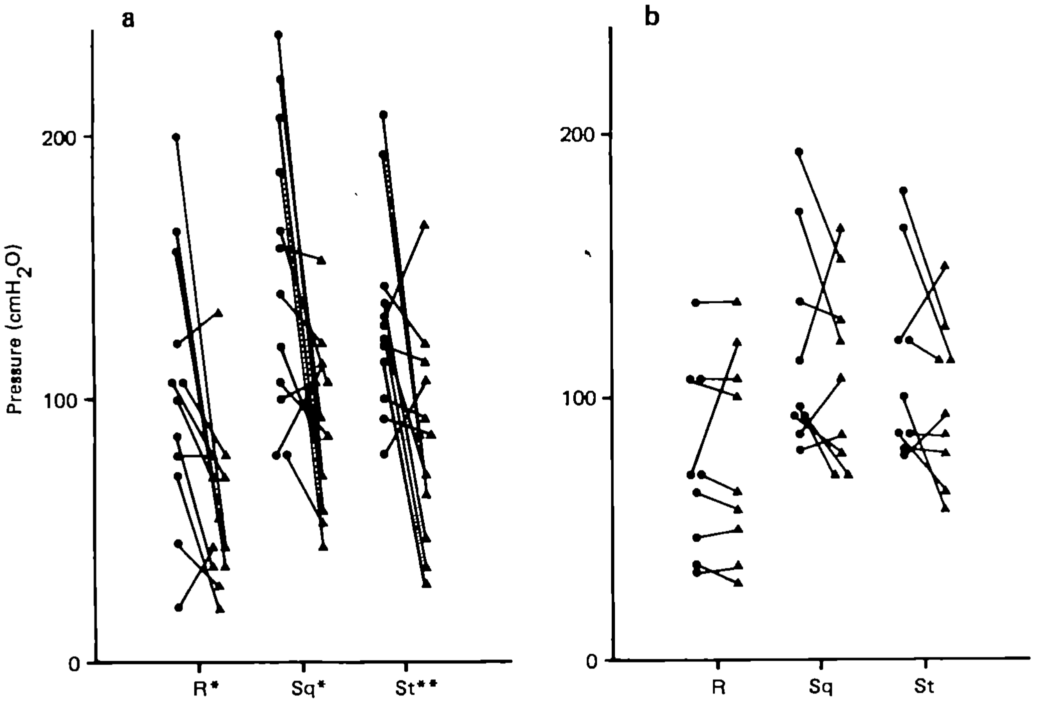

Figure 1 *Anal canal pressure at 2 cm from the anal verge before* (●) *and 3 months after* (▲) **a**, *anorectal myectomy and* **b**, *anal dilatation.* R, *resting:* Sq, *maximum pelvic floor contraction;* St, *attempted defaecation. Measurements before and 3 months after operation* **a**, *significantly different,* * P<*0·01,* ** P<*0·005;* **b**, *measurements not significantly different*

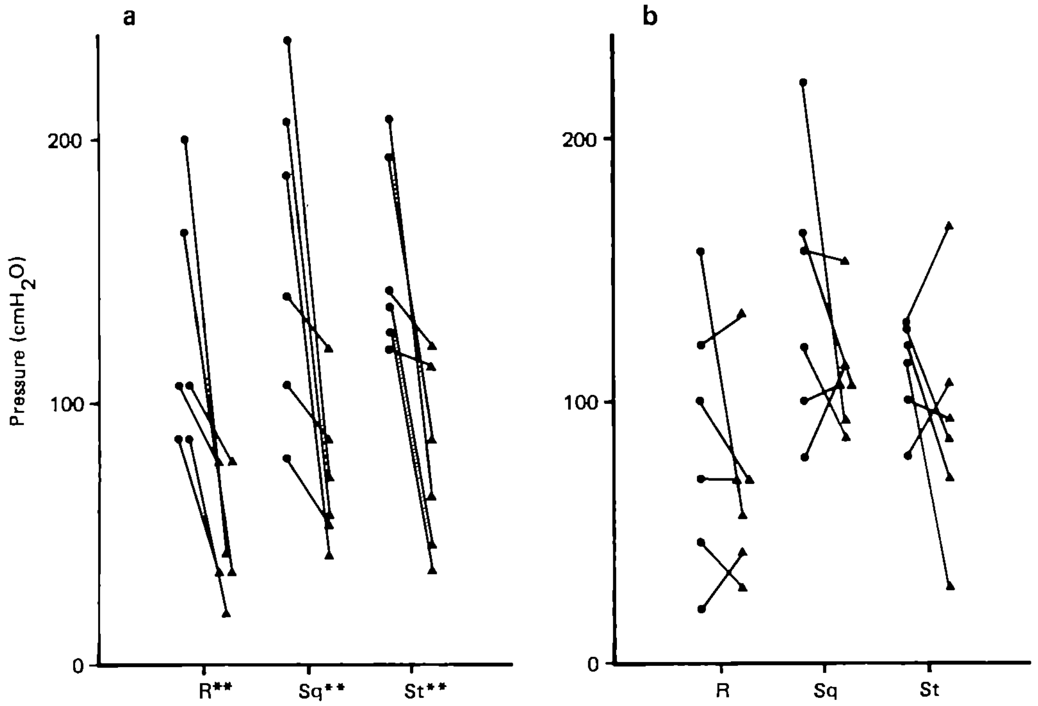

Figure 2 *Anal canal pressures before* (●) *and 3 months after* (▲) *anorectal myectomy in* **a**, *'good result' subgroup; and* **b**, *'poor result' subgroup.* R, *resting;* Sq, *maximum pelvic floor contraction;* St, *attempted defaecation. Measurements before and 3 months after operation* **a**, *significantly different,* P<*0·005;* **b**, *measurements not significantly different*

26 cm from the anal verge did not change significantly either after anorectal myectomy or anal dilatation.

Volume of first leakage during saline infusion, and total residual volume fell significantly after anorectal myectomy but no significant change was observed after anal dilatation (*Figure 4*).

The recto-anal inhibitory reflex was observed in all patients who entered this study before and after operation including the four patients who had histological evidence of short segment Hirschsprung's disease. In one patient, electromyography showed increased activity in the puborectalis during attempted defaecation before and after anorectal myectomy; despite this, operation resulted in clinical benefit. Similar observations of persistent increase in puborectalis activity on electromyography were apparent in three patients before and after anal dilatation.

Colonic transit was assessed before operation. Although the percentage of markers passed in 5 days ranged from 0 to 100 per cent, six of seven patients having a good result passed more than 60 per cent of markers, compared with only one of six patients having a poor result. The median value in the patients who achieved a good result was statistically greater than that in those who did not.

The anorectal angle did not change significantly at rest, during maximum pelvic floor contraction and attempted defaecation either after anorectal myectomy or anal dilatation (*Figure 5*). Overall rectal emptying during attempted defaecation significantly increased after anorectal myectomy, but was confined to those having a good result. There was no significant change in rectal emptying after anal dilatation (*Figure 5*).

Discussion

Functional results of anorectal myectomy have been encouraging in children with Hirschsprung's disease[5-7]. Adult patients with constipation also have been treated by anorectal myectomy. Martelli *et al.*[1] reported 62 adult patients with constipation who underwent an anorectal myectomy. In 50 patients with less than 3 stools per week, 62 per cent of these patients were able to pass 3 or more stools per week after the operation and considered themselves cured of their constipation. Anorectal myectomy also helps to exclude short segment Hirschsprung's disease, since a short aganglionic segment may be present without loss of the recto-anal inhibitory reflex. Indeed, all four patients with Hirschsprung's disease had a normal recto-anal inhibitory reflex in this study.

We have already demonstrated clinical benefit in 62 per cent of patients by anorectal myectomy but were uncertain whether

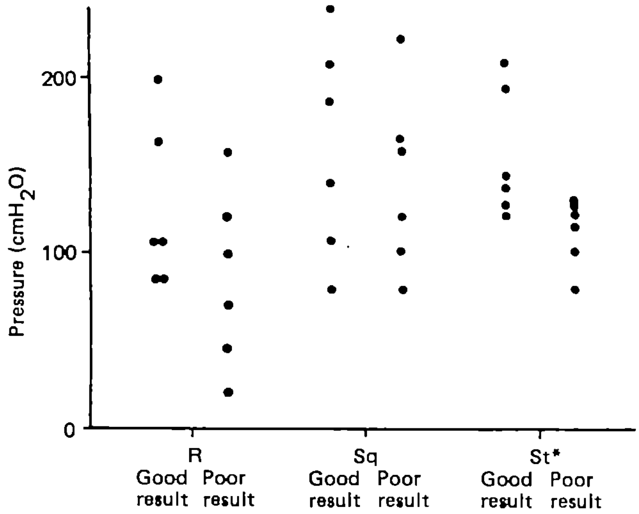

Figure 3 *Pre-operative anal canal pressures in the patients having anorectal myectomy.* R, *resting;* Sq, *maximum pelvic floor contraction;* St, *attempted defaecation,* St, * *good and poor results significantly different,* $P<0.025$; R *and* Sq, *results not significantly different*

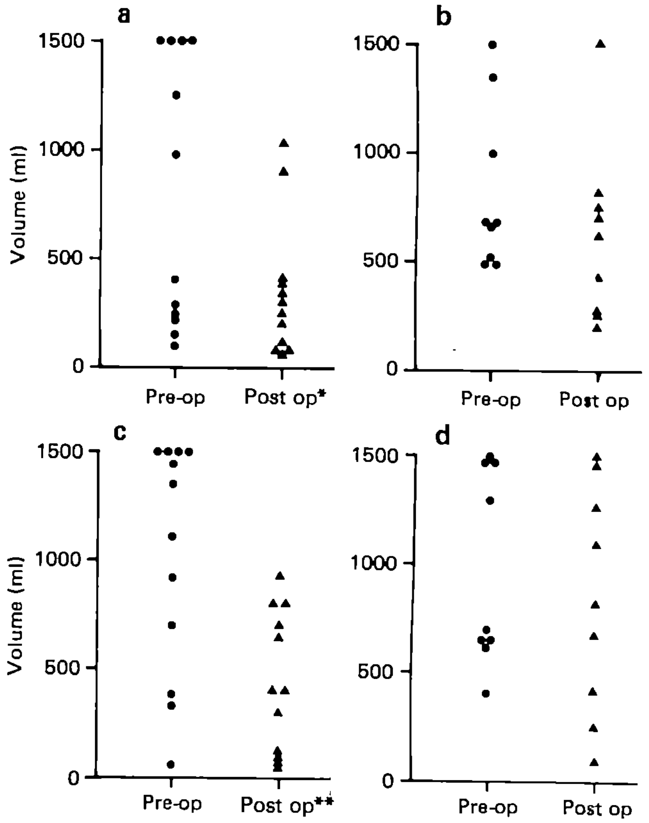

Figure 4 *First leakage volume* (a *and* b) *and total tolerable volume* (c *and* d) *before* (●) *and 3 months after* (▲) *anorectal myectomy* (a *and* c) *and anal dilatation* (b *and* d). *Pre- and postoperation results significantly different,* a *and* c, * $P<0.05$, ** $P<0.01$; b *and* d, *results not significantly different*

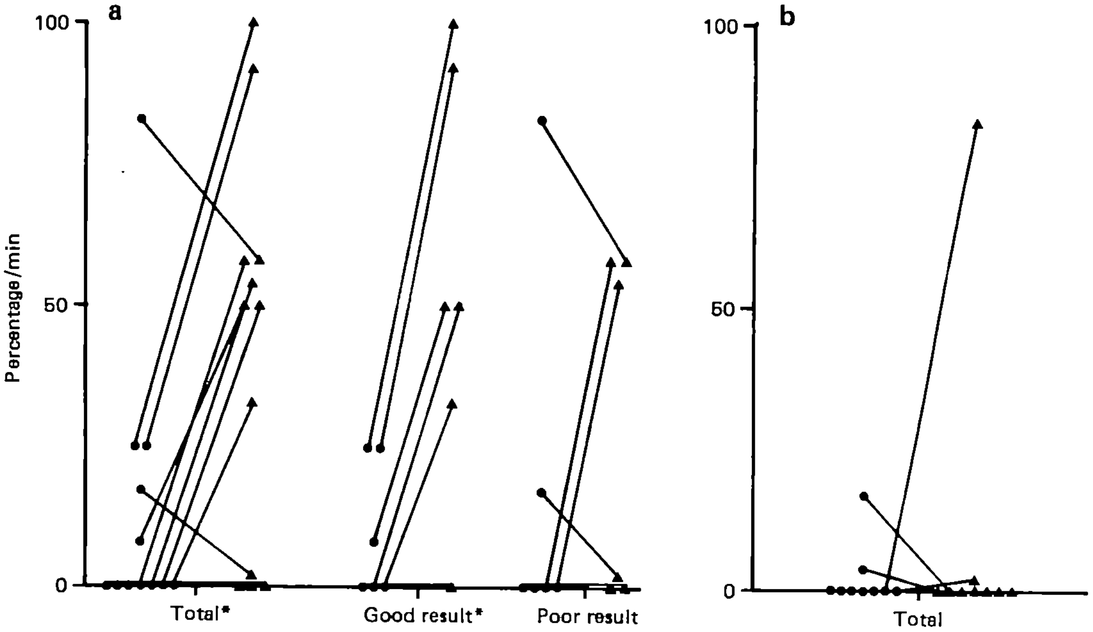

Figure 5 *Rectal emptying before* (●) *and 3 months after* (▲) a, *anorectal myectomy, and* b, *anal dilatation.* a *Total and good result, measurements before and 3 months after operation significantly different* * $P<0.025$; *poor result, measurements not significantly different;* b, *measurements not significantly different*

this improvement in bowel habit was due to anal dilatation or excision of a strip of internal anal sphincter and rectal smooth muscle[8]. We therefore compared 20 min controlled dilatation using a Park's retractor with anorectal myectomy[10].

Results of anal dilatation using the Park's anal retractor were extremely disappointing. None of the patients improved after anal dilatation and there were no changes in measurable physiological parameters either. In particular, there were no significant changes in anal pressure. This is in contrast to observations made by Hancock and others who demonstrated a significant reduction in anal pressure in both haemorrhoid and fissure patients; however, they, and others, used maximal anal dilatation rather than a controlled and prolonged 5 cm stretch with an intra-anal retractor[9,12,13]. Furthermore, the subjects reported by Hancock and others had an obvious organic abnormality in the anal canal[12]. Taylor *et al.*[10] successfully treated patients with non-Hirschsprung's megacolon, associated with raised anal canal pressures, by anal dilatation under general anaesthesia and suggested that patients should continue to use an anal dilator twice daily at home. Our study revealed that a 20 min, 5 cm anal dilatation using a Park's retractor under general anaesthesia is not associated with impaired internal or external anal sphincter damage after operation. On the other hand, 54 per cent of the patients having anorectal myectomy initially improved after the operation. The functional improvement was associated with a significant reduction of anal canal pressures at rest, during maximum pelvic floor contraction and attempted defaecation. The reduction of the anal pressures during attempted defaecation is most likely to contribute to the improvement in symptoms after anorectal myectomy. It is likely that the fall in maximum squeeze pressures was largely due to the basal component. Although there was a significant decrease in the volume of the first leakage and residual volume after anorectal myectomy, none of the patients developed incontinence[14]. Rectal emptying was significantly improved by anorectal myectomy[14].

It is possible to predict the functional result of anorectal myectomy by pre-operative measurement of anal canal pressure, colonic transit and a short history of constipation. It is likely that psychological testing will also identify patients who are unlikely to improve by operation[15]. Our study indicated that pre-operative anal canal pressure during attempted defaecation was statistically lower in patients who did badly after operation. Similarly, Taylor reported that patients with non-Hirschsprung's megacolon who had an elevated anal canal pressure were improved by anal dilatation, whilst patients with normal anal canal pressures proved more difficult to treat[10]. A simple technique for measuring colonic transit times using radio-opaque pellets has been developed, and normal subjects are able to pass more than 80 per cent of the markers within 5 days[16,17]. In our study, impaired colonic transit was more common in patients who were not improved by anorectal myectomy: six of seven patients who achieved a good result passed more than 60 per cent of markers in 5 days, compared with only one of six in those having a poor result. Anorectal myectomy would be expected to achieve a satisfactory functional result for patients with outlet obstruction. Unfortunately, measurement of colonic transit does not distinguish colonic inertia from outlet syndrome if patients are unable to open their bowels, and the use of different shapes administered over different days, with radiographs to identify the site of these markers in the colon, may overcome this objection[18].

Anorectal myectomy was subsequently performed for all patients having an unsatisfactory result after anal dilatation. So far eight of these patients have been evaluated clinically. more than 2 months after the operation and four have achieved a good result with spontaneous defaecation more than three times a week. Of the six patients who had persistent constipation after initial anorectal myectomy, two patients eventually underwent total colectomy for slow transit constipation whilst four have been managed conservatively. None of those having a colectomy and ileorectal anastomosis became incontinent despite their previous myectomy. We have experienced one recurrence of constipation, 6 months after initial anorectal myectomy, in the patients who initially achieved a good result during a follow-up between 3 and 15 months after the operation. Although further follow-up is needed for all patients having anorectal myectomy, the operation seems to play a therapeutic role in patients with constipation due to outlet obstruction.

References

1. Martelli H, Devroede G, Arhan P, Duguay C. The mechanisms of idiopathic constipation: outlet obstruction. *Gastroenterology* 1978; **75**: 623–31.
2. Wasserman IF. Puborectalis syndrome (rectal stenosis due to anorectal spasm). *Dis Colon Rectum* 1964; **7**: 87–97.
3. Preston DM, Lennard-Jones JE, Thomas BM. The balloon proctogram. *Br J Surg* 1984; **71**: 29–32.
4. Devroede G, Arhan P, Duguay C *et al.* Traumatic constipation. *Gastroenterology* 1979; **77**: 1258–67.
5. Nissan S, Bar-Maor JA, Levy E. Anorectal myectomy in the treatment of short segment Hirschsprung's disease. *Ann Surg* 1969; **170**: 969–77.
6. Thomas CG, Bream CA, Deconnick P. Posterior sphincterectomy and rectal myectomy in the management of Hirschsprung's disease. *Ann Surg* 1970; **171**: 796–810.
7. Bentley JFR, Nixon HH, Ehrenpresis TH, Spencer B. Seminar on pseudo-Hirschsprung's disease and related disorders. *Arch Dis Child* 1966; **41**: 143–7.
8. Yoshioka K, Keighely MRB. Anorectal myectomy for outlet obstruction. *Br J Surg* 1987; **74**: 373–6.
9. Hancock BD. The internal sphincter and anal fissure. *Br J Surg* 1977; **64**: 92–5.
10. Taylor I, Hammond P, Darby C. An assessment of anorectal motility in the management of adult megacolon. *Br J Surg* 1980; **67**: 754–6.
11. Farthing MMLG, Lennard-Jones JE. Sensibility of the rectum to distension reflex in ulcerative colitis. *Gut* 1978; **19**: 64–9.
12. Hancock BD, Smith K. The internal sphincter and Lord's procedure for haemorrhoids. *Br J Surg* 1975; **62**: 833–6.
13. Lord PH. A day-case procedure for the cure of third-degree haemorrhoids. *Br J Surg* 1969; **10**: 747–9.
14. Read NW, Harford WV, Schmulen AC *et al.* A clinical study of patients with faecal incontinence and diarrhoea. *Gastroenterology* 1979; **76**: 747–56.
15. Fisher SE, Keighley MRB, Brecon K, Smart V, Andrews H. Do patients with disordered defaecation have a primary personality disorder? *British Society of Gastroenterology*; September 1987.
16. Hinton JM, Lennard-Jones JE, Young AC. A new method for studying gut transit times using radioopaque markers. *Gut* 1969; **10**: 842–7.
17. Shouler P, Keighley MRB. Changes in colorectal function in severe idiopathic chronic constipation. *Gastroenterology* 1986; **90**: 414–20.
18. Bannister JJ, Timms JM, Barfield LJ, Donnelly TC, Read NW. Physiological studies in young women with chronic constipation. *Int J Colorectal Dis* 1986; **1**: 175–82.

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1130–1133

The solid bolus oesophageal egg transit test: its manometric interpretation and usefulness as a screening test

The standardized ^{99m}Tc-labelled solid bolus oesophageal egg transit test (OET) was developed for assessing oesophageal motility. Its value in detecting oesophageal motility disorders was compared with oesophageal manometry in 102 symptomatic patients. Of 32 patients with normal OET, 22 (68·8 per cent) had normal manometry, whereas of 61 patients with abnormal manometry, 51 (84 per cent) had abnormal OET ($\chi^2 = 15{\cdot}82$, $P < 0{\cdot}001$). The computer-generated condensed image of the OET clearly defined five transit patterns: normal ($n = 32$); oscillatory ($n = 21$); non-clearance ($n = 16$); 'step' delay ($n = 16$) and non-specific delay ($n = 17$). The oscillatory pattern occurred in only one patient with normal manometry, but in all six with manometrically defined achalasia and two with diffuse oesophageal spasm. The predictive value of a positive (abnormal) OET test in detecting abnormal motility (both specific and non-specific disorders) was 73 per cent, and for specific motility disorders was 100 per cent. The predictive value of a negative (normal) test in excluding specific motor disorders was 94 per cent. Manometric tertiary contractions and low amplitude waves occurred in 6/32 and 1/32 patients with normal OET but in 31/70 and 21/70 with abnormal OET ($\chi^2 = 5{\cdot}14$, $P < 0{\cdot}02$; $\chi^2 = 7{\cdot}85$, $P < 0{\cdot}001$ respectively). Patients showing oscillation demonstrated significantly more tertiary contractions (17/21) and low amplitude waves (12/21) compared with 20/81 and 10/81 patients without oscillation ($\chi^2 = 20{\cdot}47$, $P < 0{\cdot}001$; $\chi^2 = 17{\cdot}22$, $P < 0{\cdot}001$ respectively). The solid bolus oesophageal transit test provides an objective screening test of specific oesophageal motility disorders and should be performed before oesophageal manometry.

Keywords: Oesophageal motility, manometry bolus transit

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The symptoms of chest pain and dysphagia have been attributed to oesophageal motility disorders[1], and these disorders in turn are commonly associated with gastro-oesophageal reflux disease[2]. The investigation of such symptomatic patients by oesophageal manometry has been to detect specific oesophageal motor disorders, and to identify those patients at risk of developing postfundoplication dysphagia[3–5]. However, oesophageal manometry is uncomfortable to the patient, time-consuming, and requires expertise in its performance and interpretation[6].

We have previously described our development[7,8] of, and experience[9] with, the oesophageal egg transit (OET) test. This test measures the transit, whilst in the erect posture, of a labelled solid bolus through the oesophagus, and is non-invasive, objective and simple to perform. In this study, we compared the OET test with the gold standard of oesophageal manometry, and sought to assess its role as a screening test in the investigation of oesophageal motility disorders.

Patients and methods

One hundred and two consecutive patients, with symptoms suggestive of oesophageal disease, were entered into the study prospectively. There were 46 men and 56 women, and the mean age was 49·3 years (range 20–79 years). The main presenting symptoms consisted of one or more of the following: chest pain, dysphagia, heartburn and regurgitation. A detailed history was taken from each patient and the four main symptoms graded from 0 to 3 (nil, mild, moderate, severe). Non-essential medication was stopped before and during performance of the two tests. All patients underwent examination by oesophageal manometry and OET test and the results were compared.

Oesophageal manometry

Examination by oesophageal manometry was performed by the same person in each case. A triple-lumen nasogastric catheter (Portex, London, UK) was used. It had three radially spaced apertures at 5-cm intervals from its tip, and was continuously perfused by a low compliance Arndorfer pneumohydraulic infusion system (Arndorfer Medical Specialities Inc., Wisconsin, USA). Three transducers connected the Arndorfer to a multichannel recorder (Hewlitt-Packard, model 7758A, Wokingham, Berkshire, UK) and oesophageal pressure tracings were made on a polygraph. The slow station pull-through technique[10] was used to record the characteristics (length, pressure, response to swallowing) of the high pressure zone (HPZ, lower oesophageal sphincter), and motility of the oesophageal body in response to several wet swallows. Pharmacological provocation testing was not used in this study as little success has been reported in reproducing the oesophageal abnormalities[11].

Analysis of the manometric tracings included high pressure zone pressure, propagated wave amplitude and duration, and the presence of tertiary, non-propagated, contractions. The criteria used in the classification of manometric diagnoses were based on those proposed by Benjamin and colleagues[11] in 1983.

OET test

On a separate day, the OET test was performed. This required the patient to chew then swallow a 10 ml bolus of poached egg white that had been labelled with 15–20 MBq of technetium sodium pertechnetate. The test was performed in the erect posture and the patient swallowed every 20 s. Serial 1 s frames were taken by a scintillation camera for a total of 4 min, and the data were stored in an on-line computer. Activity *versus* time curves, quantifying the passage of the egg bolus, were generated for the proximal, middle and distal thirds as well as for the entire oesophagus. Having studied a cohort of healthy subjects[8], we

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Table 1 *Results of oesophageal manometry and oesophageal egg transit (OET) test in assessing oesophageal motility in 102 symptomatic patients*

	Manometry	
OET	Normal	Abnormal
Normal ($n = 32$)	22	10
Abnormal ($n = 70$)	19	51
Total ($n = 102$)	41	61

$\chi^2 = 15·82$, $P < 0·001$

have established the normal transit time for the egg bolus through the entire oesophagus to be 13–16 s. To aid in the interpretation, a computer-generated condensed image[12] was used primarily to assess the type of transit pattern so as to classify the patient into a specific transit group. To produce this image, consecutive 1 s frames of the dynamic image were condensed by the computer using a row summation technique which generated an image showing the parameters of distance travelled, time and concentration of radioisotope. The results of the OET test were reported by an assessor unaware of the manometric findings.

The analyses were performed using χ^2 2×2 tables, with Yates's correction.

Results

Of the 102 patients, 42 (41·2 per cent) experienced moderate, grade II heartburn, whilst 24 (23·5 per cent) were troubled with mild occasional heartburn. Just over half the patients (53·9 per cent) had no difficulty in swallowing, whereas 23 (22·5 per cent) presented with moderate dysphagia, requiring liquids to clear. Only 19 (18·6 per cent) patients complained of chest pain and 37 (36·3 per cent) patients were troubled with occasional mild regurgitation.

Normal oesophageal transit was demonstrated by the OET test in 32 (31·4 per cent) patients. Of these, 22 (68·8 per cent) patients showed normal oesophageal motility by manometry. There was a significant association between the results of normal OET and normal manometry on one hand, and abnormal OET and abnormal manometry on the other hand ($\chi^2 = 15·82$, $P < 0·001$, *Table 1*).

Five well-defined patterns of oesophageal transit could be classified subjectively using the condensed image (*Figure 1*). The distance travelled down the oesophagus by the egg bolus is shown on the vertical scale, and the time in seconds is along the horizontal scale. The activity–time curves allowed further objective analysis of the five patterns which were:

Type I: normal pattern (Figure 1a). The egg bolus passed rapidly and directly into the stomach. The egg bolus takes on an elongated, tear-drop shape as it passes through the oesophagus and, in this figure, the bulk of the bolus has entered the stomach, leaving part of the 'tail' in the oesophagus.

Type II: oscillatory pattern (Figure 1b). Propulsion and retropulsion of the bolus is demonstrated and, in most of these patients, the bolus did not progress down the entire oesophagus within the 4 min of the test. By widening the time scale, a clearer image of the oscillation is seen (*Figure 1c*). The periodicity of the oscillation was similar to the swallow interval of 20 s.

Type III: non-clearance pattern (Figure 1d). At the end of the 4 min of the test, part of the egg bolus still remained in the oesophagus. The criterion for clearance was that more than 90 per cent of the bolus be cleared from the area in question, be it a segment of or the entire oesophagus. Some patients displayed both non-clearance and oscillatory patterns and were thus grouped as Type II patients.

Type IV: 'step delay' pattern (Figure 1e). After an initial normal transit, there was segmental delay of some of the bolus in one part of the oesophagus, either middle or distal thirds. This was followed after a variable time delay by clearance into the stomach.

Type V: non-specific pattern (Figure 1f). Transit of the bolus through the oesophagus displayed an irregular pattern and could not be classified into one of the above four patterns.

Of the 32 patients who demonstrated a normal OET pattern, 22 (68·8 per cent) exhibited a normal oesophageal manometric profile (*Table 2*). Only two of these patients displayed manometrically defined specific motility disorders, one being diffuse oesophageal spasm and the other 'nutcracker' oesophagus. The remaining eight of these normal OET patients all had manometric patterns of a non-specific oesophageal motility disorder. Only 1 out of 21 patients who demonstrated the oscillatory OET pattern had a normal manometric tracing. However, all six patients with achalasia and two out of four with diffuse oesophageal spasm showed the oscillatory pattern, while the remainder were diagnosed as having non-specific oesophageal motor disorders. The remaining three OET patterns, Types III–V, were associated with either a normal manometric tracing or one showing a non-specific oesophageal motility disorder. Only two patients in this sub-group, one step delay and one non-clearer, showed a specific disorder on manometry.

Using oesophageal manometry as the reference standard, the predictive value of a positive OET test (i.e. an abnormal OET pattern) in detecting abnormal oesophageal motility (both specific and non-specific disorders) was 51 out of 70 (73 per cent), and in detecting a specific disorder (achalasia, diffuse oesophageal spasm, nutcracker oesophagus) was 10 out of 10 (100 per cent).

The predictive value of a negative OET test (i.e. a normal OET pattern) in detecting normal motility was 69 per cent (22/32), and in excluding specific motility disorders was substantially more accurate at 30 out of 32 (94 per cent).

Of the patients with a normal manometric tracing, the mean propagated wave amplitude was calculated to be 54·5 mmHg, with one s.d. of 29·7 mmHg. A low amplitude propagated wave was thus defined as having an amplitude of less than 24·8 mmHg (one s.d. below the mean). These low amplitude waves were suggestive of a poor contractile ability. Analysis of the OET patterns in terms of manometric parameters is shown in *Table 3*. A normal OET pattern was associated with significantly fewer low amplitude propagated waves, these being present in only 1 (3·1 per cent) of the 32 patients ($\chi^2 = 7·85$, $P < 0·001$). Low amplitude propagated waves were present in 21 (30·0 per cent) patients with an abnormal OET pattern. Tertiary contractions were present in 6 (18·8 per cent) and 31 (44·3 per cent) patients with normal and abnormal OET patterns respectively ($\chi^2 = 5·14$, $P < 0·02$). The oscillatory OET pattern was associated with a significantly greater number of low amplitude propagated waves ($\chi^2 = 17·22$, $P < 0·001$) and significantly more tertiary contractions ($\chi^2 = 20·47$, $P < 0·001$) than the non-oscillatory OET patterns. The remaining three OET patterns (non-clearance, step delay, non-specific) showed no significant association with either low amplitude propagated waves or the presence of tertiary contractions. There was no relationship between any of the OET patterns and the manometric parameters of either HPZ pressure or duration of propagated waves.

Using Kendall's τ rank correlation coefficient, no significant correlation was encountered between any of the OET patterns and the grade of presenting symptoms.

Discussion

The investigation by oesophageal manometry of a patient with a suspected oesophageal motor disorder is a tedious process. The presence of a nasogastric catheter reduces the patient tolerance and the time taken to complete the test[13] can be as long as 2 h.

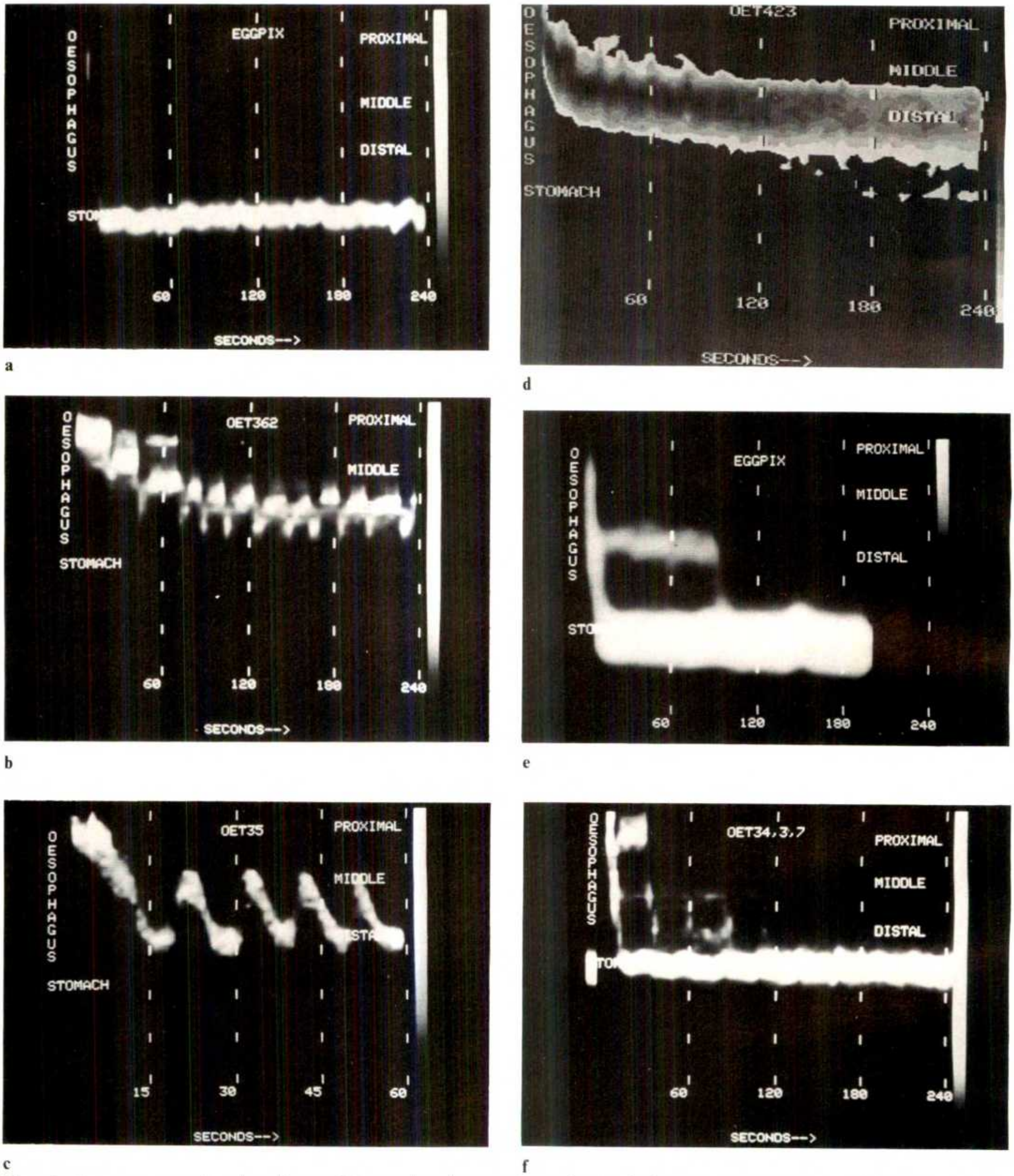

Figure 1 *Computer-generated condensed image of the oesophageal egg transit test showing the five transit patterns:* **a** *I: normal;* **b** *II: oscillatory;* **c** *detailed pattern of oscillatory;* **d** *III: non-clearance;* **e** *IV: step delay;* **f** *V: non-specific pattern (see text for descriptions)*

The low diagnostic yield of specific motility disorders (11·8 per cent in our study) makes it of questionable cost-effectiveness, yet it has been advocated in the pre-operative identification of patients who may be at risk of developing postfundoplication obstructive symptoms[3,4]. The usefulness of oesophageal manometry in the clinical setting has previously been argued[6,14,15].

The OET test is a simple test to perform, and takes only 4 min. The reproducibility of the test is good[8] (coefficient of variation of the total transit of 14 per cent), and the patient tolerance is excellent. It is reported using two methods. Firstly, the activity–time curves provide objective quantification of the oesophageal transit. As the labelled egg passes down through the oesophagus, it takes on an elongated shape. Thus, the bolus is present in more than one segment of the oesophagus at the same time. As previously stated, the time for clearance through a particular segment is when more than 90 per cent of the bolus is cleared through that segment. Thus, the transit times through two segments may be the same. It is, therefore, important to note that the time for total oesophageal transit is not the

Table 2 *Comparison of motility patterns of 102 symptomatic patients by oesophageal manometry and OET*

	Oesophageal manometry				
OET	Normal ($n=41$)	Achal-asia ($n=6$)	DOS ($n=4$)	Nut-cracker ($n=2$)	NOMD ($n=49$)
Normal ($n=32$)	22	—	1	1	8
Oscillatory ($n=21$)	1	6	2	—	12
Step delay ($n=16$)	9	—	—	1	6
Non-clearer ($n=16$)	3	—	1	—	12
Non-specific ($n=17$)	6	—	—	—	11

DOS, diffuse oesophageal spasm; NOMD, non-specific oesophageal motility disorder

Table 3 *OET patterns in manometric terms*

	Propagated wave low amplitude		Tertiary contractions	
	Present	Absent	Present	Absent
Normal OET ($n=32$)	1*	31	6†	26
Abnormal OET ($n=70$)	21*	49	31†	39
Oscillatory ($n=21$)	12‡	9	17§	4
Non-oscillatory ($n=81$)	10‡	71	20§	61

* $\chi^2=7{\cdot}85$; $P<0{\cdot}001$; † $\chi^2=5{\cdot}14$; $P<0{\cdot}02$; ‡ $\chi^2=17{\cdot}22$; $P<0{\cdot}001$; § $\chi^2=20{\cdot}47$; $P<0{\cdot}001$

summation of the times for the proximal, middle and distal thirds. A problem with measurement of transit times using the activity–time curves is that an initial double or multiple swallow makes quantification of transit impossible. This can be theoretically overcome with deconvolutional analysis[16] but, in practice, the amount of noise introduced by this method makes it impractical. In these cases, reliance is made on the condensed image of oesophageal transit. This second method of reporting, with the condensed image, provides an overall assessment of the transit and hence the motility. As these results show, there are five well-defined patterns of oesophageal transit. All patients can easily be classified into one of these patterns, and the exact times of transit provide additional objective information.

The normal and abnormal OET patterns were significantly associated with the normal and abnormal manometric tracings, respectively. In terms of manometric diagnoses, the normal OET pattern was more frequently associated with normal manometry, and the patients in this group with abnormal manometry were largely confined to non-specific oesophageal motility disorders. In contrast, only 1 out of the 21 patients with an oscillatory OET pattern had normal manometry. The remainder of the oscillatory patients all showed manometric abnormalities, and included the six patients with manometrically diagnosed achalasia. Closer inspection of these oscillatory patients, revealed that they demonstrated a significantly greater number of low amplitude, poor contractile, propagated waves and significantly more tertiary, non-propagated contractions. The remaining three OET patterns, that of non-clearance, step delay and the non-specific pattern, were associated with either normal manometry or non-specific manometric abnormalities. As a rule, patients with specific motor disorders did not demonstrate any of these three latter OET patterns.

The OET test was extremely accurate in detecting and excluding the specific motility disorders of achalasia, diffuse oesophageal spasm and nutcracker oesophagus, with predictive rates of 100 per cent and 94 per cent, respectively. The demonstration of such disorders identifies which patients would require more detailed investigation. For the detection of abnormal motility in general, the OET test was not as accurate, because of the poorer association between the findings of the OET and the presence or absence of non-specific motility abnormalities.

In conclusion, the OET test is a useful non-invasive test of oesophageal motility. All patients can be classified into one of five transit patterns and its ability to detect or exclude a specific oesophageal motor disorder is extremely high. We feel that this simple investigation should be used as a screening test for suspected oesophageal dysmotility and should be performed before oesophageal manometry. In these circumstances, a presenting patient would first undergo investigation with the OET test. If a Type II oscillatory transit pattern was encountered, this patient would be referred for oesophageal manometry. Owing to the recognized association of abnormal oesophageal motility with gastro-oesophageal reflux disease[2], a patient who exhibited one of OET Types III–V (step delay, non-clearance, non-specific) should undergo examination by 24 h oesophageal pH monitoring in order to identify a possible cause for the abnormal motility. Depending on the symptomatology, other patients (but not necessarily all) with a Type I normal OET pattern would require oesophageal pH monitoring. The exact times of transit through the segments of the oesophagus, as shown by the activity–time curves, are also useful in assessing the effect of treatment on the oesophageal transit.

References

1. Davies HA, Rhodes J. How often does the gut cause anginal pain? *Acta Med Scand* 1981; **644** (Suppl): 62–5.
2. Baldi F, Ferrarini F, Cassan M *et al.* Manometric evaluation of the oesophageal peristalsis and of the lower oesophageal sphincter in reflux oesophagitis. *Ital J Gastroenterol* 1982; **14**: 145–9.
3. Pope CE. II: Esophageal motility—who needs it? *Gastroenterology* 1978; **74**: 1337–8.
4. DeMeester TR. Surgical management of gastroesophageal reflux. In: Castell DO, Wu WC, Ott DJ, eds. *Gastroesophageal Reflux Disease*. London: Futura, 1985: 243–80.
5. Blackwell JN, Castell DO. Oesophageal motility—recent advances and implications. *Clin Sci* 1984; **67**: 145–51.
6. Duranceau AC, Devroede G, Lafontaine E, Jamieson GG. Esophageal motility in asymptomatic volunteers. *Surg Clin N Am* 1983; **63**: 777–86.
7. Cranford CA, Sutton D, Kennedy N, Cuschieri A. Oesophageal transit time: a new technique using a radio-labelled solid egg white bolus. *Br J Surg* 1985; **72**: (Abstract) 1037.
8. Cranford CA, Sutton D, Sadek SA, Kennedy N, Cuschieri A. New physiological method of evaluating oesophageal transit. *Br J Surg* 1987; **74**: 411–15.
9. Eriksen CA, Sadek SA, Cranford CA, Sutton D, Kennedy N, Cuschieri A. Solid bolus oesophageal transit in patients with reflux oesophagitis. *Br J Surg* 1986; **73**: 496.
10. Welsh RW, Drake JT. Normal lower esophageal pressure: A comparison of rapid versus slow pull-through techniques. *Gastroenterology* 1980; **78**: 1446–51.
11. Benjamin SB, Richter JE, Cordova CM, Knuff TE, Castell DO. Prospective manometric evaluation with pharmacologic provocation of patients with suspected esophageal motility dysfunction. *Gastroenterology* 1983; **84**: 893–901.
12. Klein HA, Wald A. Computer analysis of radionuclide oesophageal transit studies. *J Nucl Med* 1984; **25**: 957–64.
13. Bancewicz J, Osugi H, Marples M. Clinical implications of abnormal oesophageal motility. *Br J Surg* 1987; **74**: 416–17.
14. Meshkinpour H, Glick ME, Sanchez P, Tarvin J. Esophageal manometry—a benefit and cost analysis. *Dig Dis Sci* 1982; **27**: 772–5.
15. Clouse RE, Staiano A. Contraction abnormalities of the esophageal body in patients referred for esophageal manometry. *Dig Dis Sci* 1983; **28**: 784–91.
16. Nimon CC, Lee TY, Britton KE, Granowska M, Grunewald S. Practical application of deconvolution techniques to dynamic studies. In: *Medical Radionuclide Imaging*. International symposium, Heidelberg 1980, I.A.E.A. Vienna, 1981; 367–88.

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Periodic gallbladder contraction maintains bile acid circulation during the fasting period: a canine study

Using a canine model we have studied the relationship between the interdigestive cycle in the small intestine, motility changes in the biliary tract and bile acid output into the duodenum from direct hepatic secretion and gallbladder emptying. Under anaesthesia catheters were inserted into the gallbladder, common bile duct and duodenum, and electrodes were attached to the small intestine in five dogs. These animals were subsequently studied conscious and fasting. A double marker technique was used to measure bile acid output from the gallbladder and liver while pressure in the gallbladder and common bile duct and electrical activity in the small intestine were monitored. Four complete interdigestive cycles were recorded in each dog. Output of bile acids from the gallbladder fluctuated with the phases of the cycle: being lowest in phase I (3·9 ± 0·7 μmol/min); increasing significantly ($P<0{\cdot}005$) *in phase II (9·8 ± 1·0 μmol/min); remaining elevated in phase III (13·9 ± 1·7 μmol/min); and falling significantly* ($P<0{\cdot}05$) *in phase IV (8·4 ± 1·8 μmol/min). In contrast, hepatic secretion of bile acids directly into the duodenum remained fairly constant. Intraluminal pressure in the biliary tract paralleled the fluctuation in gallbladder bile acid output, being significantly increased* ($P<0{\cdot}05$) *in phases II and III. Periodic contraction of the gallbladder would, therefore, appear to be the principal mechanism for the phasic output of bile during fasting.*

Keywords: Gallbladder contraction, bile secretion, migrating myo-electric complex

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The solubility of cholesterol in bile is determined by the relative concentrations of cholesterol, phospholipids and bile acids[1]. Bile acids are normally conserved by the body, being returned to the liver via the enterohepatic circulation. During fasting most of the bile acid pool becomes sequestered in the gallbladder and bile secreted by the liver at this time is frequently supersaturated with cholesterol[2,3]. However, a small portion of the bile acid pool continues to circulate in the enterohepatic circulation during the interdigestive period[4]; this is probably critical in maintaining cholesterol solubility at this time. The entry of bile acids into the duodenum during fasting is phasic and is closely coordinated with the interdigestive cycle in the small intestine[5,6]. Periodic contraction of the gallbladder[7,8], fluctuation in the rate of hepatic secretion[9,10], and cyclic changes in sphincter of Oddi motility[11,12] have all been suggested as possible mechanisms for this phasic output of bile during fasting.

The periodic contraction of the gallbladder, in rhythm with the interdigestive cycle in the small intestine, was first shown by Itoh[7] using force transducers sutured to the wall of the gallbladder in dogs. It has since been confirmed by ultrasonography[13] and cholescintigraphy[14] that these interdigestive gallbladder contractions also occur in man. No attempt was made in these studies to correlate gallbladder contraction with bile acid output. Other studies on the hepatic secretion of bile acids in relation to the interdigestive cycle have usually been conducted on cholecystectomized animals and humans[9,10].

In the present study, the outflow of bile acids from gallbladder emptying and direct hepatic secretion were quantified and correlated with pressure changes in the gallbladder and common bile duct during each phase of the interdigestive cycle. This experimental model allowed the output of bile acids from the gallbladder and liver and the dynamics of bile flow to be studied simultaneously without disrupting the integrity of the biliary tract or disturbing the sphincter of Oddi or the continuity of the bowel. A canine model was selected for study because the anatomy of the extrahepatic biliary tract and patterns of bile acid secretion and intestinal motor activity in the interdigestive period are similar to those in man.

Materials and methods

Surgical preparation

Five healthy female mongrel dogs each weighing 20–25 kg were surgically prepared under sodium pentobarbital anaesthesia (30 mg/kg body weight). Using a sterile technique, the abdomen was opened through a midline incision and the gallbladder, duodenum and small intestine were exposed. The tips of two polyethylene catheters (ID 0·86 mm) were introduced into the gallbladder through stab incisions in the fundus and secured by suturing a narrow plastic flange on each catheter to the serosa of the gallbladder. A single polyethylene catheter (ID 0·86 mm) was introduced into the common bile duct through the right lateral hepatic duct, as described by Doyle[15]. Three polyethylene catheters were inserted into the duodenum through a small duodenotomy 2 cm distal to the pylorus; these were positioned so that the tip of the proximal catheter (ID 0·86 mm) lay in the first part of the duodenum, the tip of the second catheter (ID 0·86 mm) lay at the level of the papilla of Vater and the tip of the distal catheter (ID 3·0 mm) lay at the level of the ligament of Treitz. A single catheter (ID 0·86 mm) was introduced through a small enterostomy 50 cm distal to the ligament of Treitz and its tip secured a further 5 cm distally. All catheters were exteriorized through a stainless steel port positioned in the right abdominal wall. The outer end of each catheter was occluded and the port covered by a protective cap.

Three monopolar silver electrodes were sutured to the serosal surface of the small intestine; the first of these was attached to the

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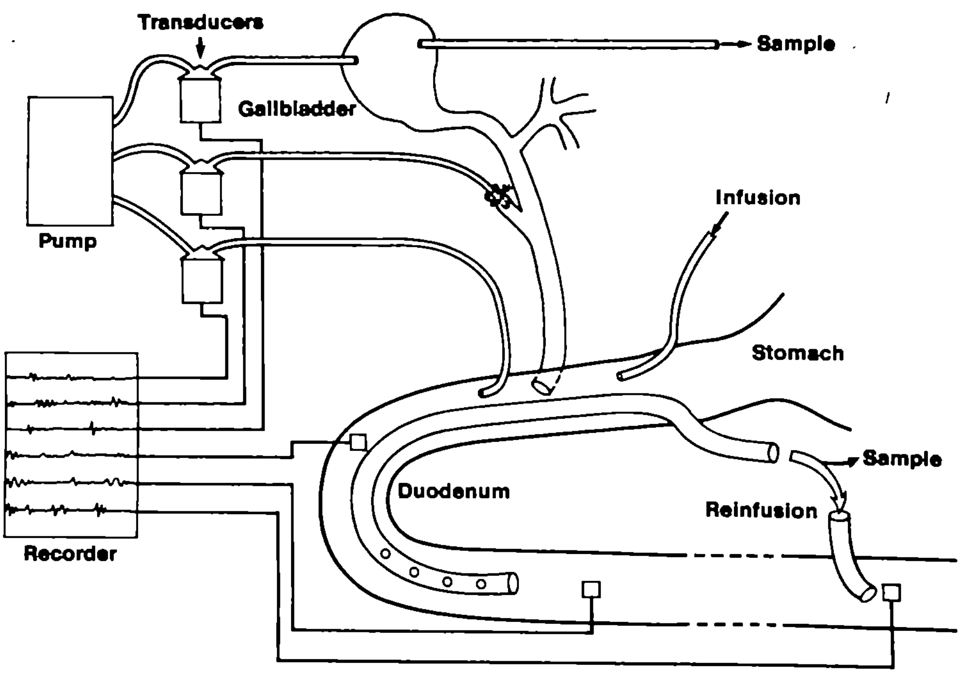

Figure 1 *Schematic diagram of method used to measure output of bile acids from the gallbladder and liver into the duodenum and record pressure in the biliary tract and electrical activity in the small intestine*

duodenum at the level of its junction with the common bile duct, the second and third were attached to small intestine on its antimesenteric border at points 70 and 140 cm, respectively, distal to the first electrode. Each electrode was connected by insulated stainless steel wire to a multipin electrical connector in a second stainless steel port positioned in the left abdominal wall.

After recovery from anaesthesia, water was allowed *ad libitum* and a normal diet of commercial dog food ('Pow-R-Pac', New-Life Feeds, Calgary, Alberta) 600 g/day resumed on the second or third postoperative day. At least 3 weeks was allowed for recovery from surgery before commencing tests.

Experimental procedure

Before each study, the dog was fasted for 24 h; water was allowed *ad libitum* but was discontinued at least 4 h before the study period. During the test the animal stood in a Pavlov sling in a quiet room. Leads from the multipin electrical connector were attached via a.c. couplers (9806A, Beckman, Schiller Park, Illinois) to a polygraph recorder (RM Dynograph, Beckman, Schiller Park, Illinois). A fourth lead, attached to the body of the stainless steel port, acted as the indifferent electrode during recordings. The input signal was attenuated by a 30 Hz high frequency filter; a time constant of 1 s was used. By continuously monitoring electrical activity in the small intestine the various phases of the interdigestive cycle were immediately identified using criteria established by Code and Marlett to define each phase[16]. Phase I, the quiet phase, is characterized by regular slow waves with a frequency of about 18 waves/min. During phase II irregular spikes or action potentials are superimposed on some of these slow waves. In phase III, a period of intense contractile activity, each slow wave is accompanied by at least one, and often several, action potentials. This band of activity is propagated slowly down the small intestine as the migrating myoelectric complex. Phase IV is another period of irregular spike activity leading to the return of the quiescent phase I.

One of the gallbladder catheters, the common bile duct catheter and the second duodenal catheter were attached by polyethylene tubing (ID 0·86 mm) to three pressure transducers (P-23BB, Statham, Hato Rey, Puerto Rico), the output from which was displayed on the polygraph recorder (*Figure 1*). A minimally compliant pneumohydraulic capillary infusion system, similar to that described by Arndorfer[17], was also attached to each catheter assembly; normal saline was infused through this at the rate of 0·1 ml/min. In estimating pressure in the gallbladder and common bile duct, the duodenal pressure in the quiet phase of the interdigestive cycle was taken as the zero reference.

The output of bile acids into the duodenum during each phase of the cycle was estimated by duodenal perfusion which was commenced at least 1 h before the study period. The perfusing solution containing [*methoxy*-^{3}H]methoxyinulin (N.E.N., N. Billerica, Massachusetts) in normal saline (0·1 mCi/l) was warmed to 37°C and infused through the proximal duodenal catheter at a rate of 2·4 ml/min using an infusion pump. Duodenal contents were aspirated continuously through the distal duodenal catheter, pooled every 5 min, and a sample (0·5 ml) retained for analysis. To prevent depletion of bile acids the remainder of the duodenal aspirate was re-infused into the jejunum at the rate of 2·4 ml/min; preliminary studies using a dye confirmed that no reflux from the jejunum into the duodenum occurred at this re-infusion rate.

During the quiescent phase of the interdigestive cycle in the duodenum approximately 1 ml of bile was withdrawn from the gallbladder, labelled by the addition of a second radioactive marker [*carboxyl*-^{14}C]carboxylinulin (N.E.N., N. Billerica, Massachusetts) 5 mCi in 0·1 ml, and returned to the gallbladder through the pressure recording catheter. This was then thoroughly mixed with gallbladder contents by gentle aspiration and re-infusion with a syringe. Every 5 min throughout the study period a sample (0·25 ml) of bile was withdrawn from the gallbladder through the other catheter. To ensure that this was representative of gallbladder contents 2 ml were first withdrawn to clear the dead space in the tubing; this was returned to the gallbladder after sampling.

All samples were analysed for bile acids by 3α-hydroxysteroid assay[18]. Aliquots from each sample were also assayed for radioactivity on a liquid scintillation counter (LS 6800, Beckman, Schiller Park, Illinois) using an external standard and quench correction factor to determine DPM values for [^{3}H] and [^{14}C].

Data analysis

The volume of flow through the duodenum during each 5 min period was estimated by the degree of dilution of the marker [*methoxy*-^{3}H]methoxyinulin ([^{3}H]MI) in each duodenal sample using the formula:

$$DV = \frac{[[^3\text{H}]\text{MI}]_\text{I} \times V_\text{I}}{[[^3\text{H}]\text{MI}]_\text{A}}$$

in which DV is the volume of duodenal flow, $[[^3\text{H}]\text{MI}]_\text{I}$ is the concentration of [^{3}H]MI in the duodenal infusate, V_I the volume of duodenal infusate and $[[^3\text{H}]\text{MI}]_\text{A}$ the concentration of [^{3}H]MI in the duodenal aspirate. The output of the gallbladder marker [*carboxyl*-^{14}C]carboxylinulin ([^{14}C]CI) into the duodenum during this time was estimated by multiplying the concentration of this marker, $[[^{14}\text{C}]\text{CI}]_\text{A}$, in each duodenal sample by the volume of duodenal flow:

$$[^{14}\text{C}]\text{CI output} = [[^{14}\text{C}]\text{CI}]_\text{A} \times DV$$

The output of bile acids into the duodenum was similarly estimated using the formula:

$$\text{total } BA \text{ output} = [\text{BA}]_\text{A} \times DV$$

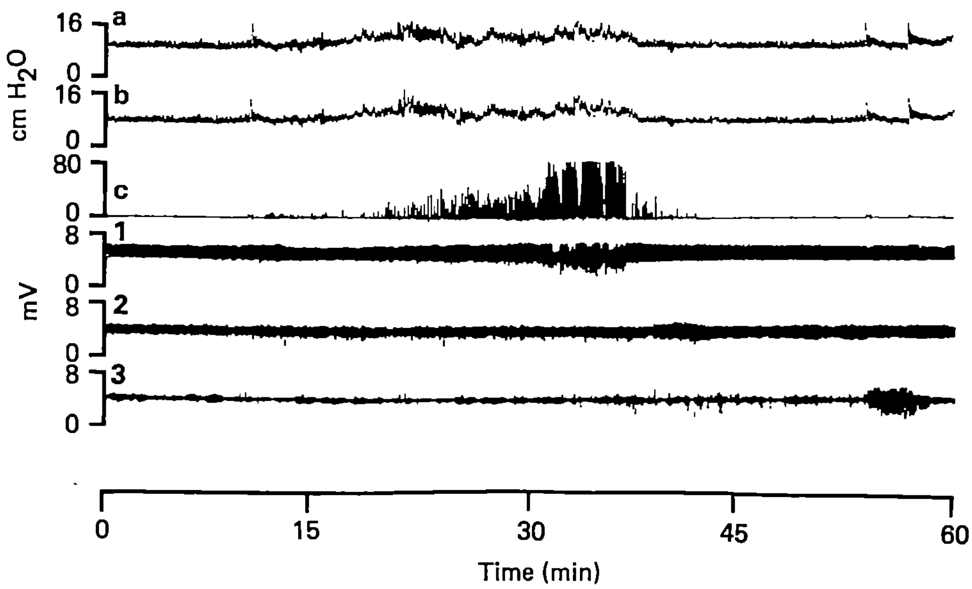

Figure 2 *Recording of intraluminal pressure in* **a** *gallbladder,* **b** *common bile duct and* **c** *duodenum and electrical activity in the small intestine (electrodes 1, 2 and 3) during one interdigestive cycle*

in which total *BA* output is the total output of bile acid from the liver and gallbladder into the duodenum during each sampling interval and $[\mathrm{BA}]_A$ is the bile acid concentration in the duodenal aspirate.

A method previously described in a primate model[19] was used to determine the relative contributions of gallbladder emptying and direct hepatic secretion to total bile acid output. To estimate the portion coming from the gallbladder the ratio of bile acids to $[^{14}\mathrm{C}]\mathrm{CI}$ was determined in each sample of bile obtained from the gallbladder; this ratio will be identical in gallbladder bile entering the duodenum at this time. The output of bile acids from the gallbladder during each sampling interval was estimated using the formula:

$$\mathrm{GB}\ BA\ \mathrm{output} = [^{14}\mathrm{C}]\mathrm{CI\ output} \times \frac{[\mathrm{BA}]_{\mathrm{GB}}}{[[^{14}\mathrm{C}]\mathrm{CI}]_{\mathrm{GB}}}$$

in which GB *BA* output is the output of bile acids from the gallbladder, $[\mathrm{BA}]_{\mathrm{GB}}$ the concentration of bile acids in the gallbladder and $[[^{14}\mathrm{C}]\mathrm{CI}]_{\mathrm{GB}}$ the concentration of $[^{14}\mathrm{C}]\mathrm{CI}$ in the gallbladder. The difference between the total output of bile acids and the output from the gallbladder represented hepatic secretion of bile acids directly into the duodenum:

$$\text{hepatic secretion into duodenum} = \text{total } BA \text{ output} - \text{GB } BA \text{ output}$$

Four complete interdigestive cycles were recorded in each of the five dogs and the mean rates of bile acid output (μmol/min) from the liver and gallbladder during each phase determined. Student's *t* test for paired data was used to analyse differences between the rates of output of bile acids in consecutive phases of the cycle. Differences in pressure in the gallbladder and common bile duct between consecutive phases of the cycle, and pressure differences between the gallbladder and common bile duct in individual phases were similarly analysed.

Results

Interdigestive cycle

The mean duration of phases I to IV of the interdigestive cycle in the duodenum was 25·0±8·1, 54·3±8·6, 6·3±0.6 and 7·0±0·7 min (mean±s.e.m.), respectively, using established criteria[16] to define each phase.

Gallbladder and common bile duct pressure

Throughout the cycle pressures in the gallbladder and common bile duct (CBD) remained very similar and their waveforms almost identical (*Figure 2*). During phase I both remained fairly steady, the mean pressures observed during this phase were 7·3±0·9 and 6·2±1·3 $\mathrm{cmH_2O}$, in the gallbladder and CBD respectively. With the onset of phase II activity in the duodenum, irregular oscillations in pressure (±2 $\mathrm{cmH_2O}$) were observed simultaneously in the gallbladder and common bile duct; the mean pressures recorded in the gallbladder and CBD during this phase (8·1±0·9 and 7·3±1·4 $\mathrm{cmH_2O}$, respectively) were both significantly higher ($P<0{\cdot}05$) than those observed during phase I. These pressure waves continued into phase III during which mean pressures remained elevated (gallbladder 9·3±1·0 $\mathrm{cmH_2O}$, CBD 8·1±1·5 $\mathrm{cmH_2O}$). With the onset of phase IV in the duodenum these fluctuations in pressure ceased; gallbladder mean pressure during this phase (6·7±0·6 $\mathrm{cmH_2O}$) was significantly lower ($P<0{\cdot}05$) than that in phase III; CBD mean pressure also fell (5·9±1·3 $\mathrm{cmH_2O}$), but this was not significant ($P=0{\cdot}06$). No significant pressure difference was observed between the gallbladder and CBD in any phase of the cycle.

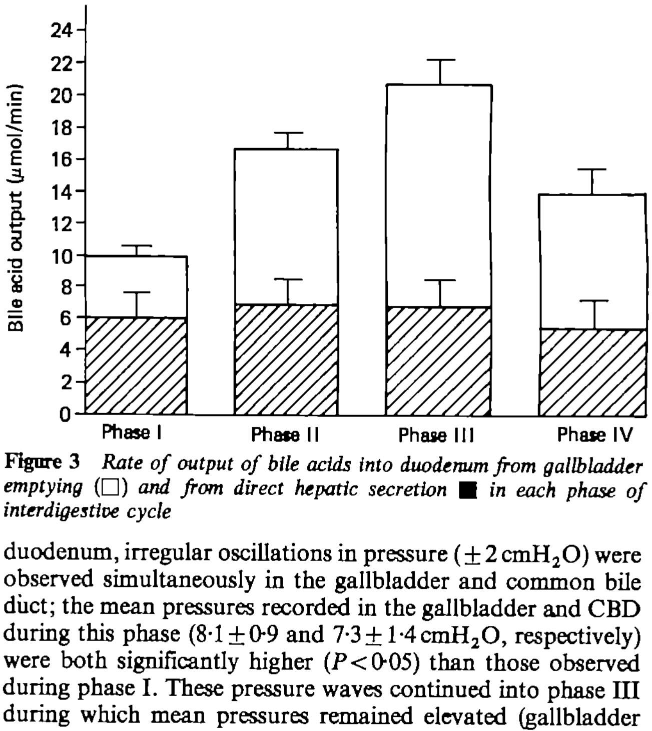

Figure 3 *Rate of output of bile acids into duodenum from gallbladder emptying (☐) and from direct hepatic secretion* ■ *in each phase of interdigestive cycle*

Bile acid output

During each complete cycle a total of 1227±99 μmol bile acids entered the duodenum; 681±52 μmol (55·5 per cent) of this came from the gallbladder and 546±98 μmol (44·5 per cent) from direct hepatic secretion. A periodic pattern of bile acid output in the interdigestive cycle was demonstrated with significantly increased ($P<0{\cdot}05$) output in phases II and III (*Figure 3*). This fluctuation in bile acid output was attributable solely to variation in the output from the gallbladder. Changes in the rate of output from the gallbladder closely paralleled pressure changes in the biliary tract. Output from the gallbladder was lowest in phase I (3·9 ± 0·7 μmol/min); this increased significantly ($P<0\cdot005$) in phase II (9·8 ± 1·0 μmol/min), remained elevated in phase III (13·9 ± 1·7 μmol/min), and significantly fell ($P<0\cdot05$) in phase IV (8·4 ± 1·8 μmol/min). In contrast, the secretion of bile acids by the liver directly into the duodenum remained fairly constant throughout the cycle, being 6·0 ± 1·9, 6·9 ± 1·7, 6·8 ± 1·9 and 5·5 ± 1·9 μmol/min in phases I to IV, respectively.

Discussion

Periodic contraction of the gallbladder[7,8], fluctuation in the rate of hepatic secretion[9,10] and cyclic changes in sphincter of Oddi motility[11,12] have all been suggested as possible mechanisms for the phasic output of bile during fasting. Our findings suggest that periodic gallbladder contraction is the principal mechanism, for we have demonstrated that the gallbladder contracts and empties intermittently in rhythm with the interdigestive cycle in the small intestine. In contrast, the secretion of bile acids by the liver directly into the duodenum remained fairly constant. This latter finding is at variance with the reports of others[9,10] who described a phasic pattern of hepatic bile acid secretion in cholecystectomized dogs and humans. The pattern of secretion of bile acids by the liver may have been affected by removal of the gallbladder in those studies as cholecystectomy is known to influence the size, composition and turnover of the bile acid pool[20–22]. Our results on the partitioning of bile between the gallbladder and duodenum are comparable to those obtained by others using non-invasive methods[14,23]. Ryan[23], using a modified cholescintigraphic technique to study bile flow in conscious dogs, noted a phasic pattern of gallbladder emptying and a continuous pattern of hepatic secretion with nearly one half of the bile secreted by the liver entering the intestine during each interdigestive cycle.

It has been suggested that changes in sphincter of Oddi motility might regulate bile flow in the interdigestive period[11]. Cyclical electrical and motor activity have been demonstrated at this sphincter in rhythm with the interdigestive cycle in the duodenum[12,24].

Changes in sphincter tone alone could not have accounted for the periodic outflow of bile from the gallbladder in our study as the secretion of bile acids by the liver directly into the duodenum remained fairly constant. The sphincter of Oddi is also traversed by the terminal pancreatic duct in man; while pancreatic exocrine secretion also fluctuates with the interdigestive cycle the peak does not coincide with the peak in bile acid output[6,25]. This would suggest that the sphincter of Oddi is not the principal regulator of bile flow in the interdigestive period though it is possible that the rate of flow could be modulated by changes in sphincter tone. Irregular oscillations in pressure were observed simultaneously in the gallbladder and common bile duct throughout phases II and III in all out studies; it is likely that these represented gallbladder contractions rather than sphincter of Oddi activity as gallbladder emptying increased significantly during these phases.

The cystic duct also possesses sphincter-like properties[26]; because of its unique location small changes in its diameter could have a considerable effect on the flow of bile in and out of the gallbladder. Although minor differences in pressure between the gallbladder and common bile duct were observed, no significant pressure gradient across the cystic duct could be demonstrated in any phase of the cycle; this, together with the simultaneous and identical oscillations in pressure seen in the gallbladder and common bile duct, would suggest that active constriction of the cystic duct is not a major factor in determining the pattern of bile flow in the interdigestive period. A pressure gradient, however small, must exist between the common bile duct and gallbladder at some stage for filling of the gallbladder to occur. It has been shown by other methods[13,14,27] that filling occurs principally during phases IV and I. As we had no marker of gallbladder filling we were unable to confirm this; however, the reduction in mean gallbladder pressure, absence of contractions, and reduced output of bile acid from the gallbladder seen in phases IV and I would all favour gallbladder filling at this time.

Our findings suggest that periodic contraction of the gallbladder is the principal mechanism for the phasic output of bile acids in the interdigestive cycle. In keeping with the concept of the interdigestive 'housekeeper'[16] these bile acids probably act to hydrolyse fatty food remnants and cellular debris in the digestive tract. The associated migrating myo-electric complex sweeps these bile acids to their site of absorption in the terminal ileum. The secretory and motor components of the interdigestive cycle both serve to maintain the enterohepatic circulation of bile acids during fasting which is important in maintaining cholesterol solubility at this time. These contractions may also prevent the hyperconcentration of solutes in the gallbladder by emptying it of concentrated viscous bile and enabling it to refill with dilute hepatic bile. Additionally, they may rid the gallbladder of microcrystals formed between meals.

In the majority of patients with cholesterol gallstones, supersaturation of bile appears to result from alterations in the enterohepatic cycling of bile acids[28]. As the gallbladder is the only part of the enterohepatic circulation capable of sequestering bile acids and contains most of the bile acid pool during fasting[29] even minor changes in its motility could have far reaching effects on cholesterol solubility. It has been shown that the size of the bile acid pool, rate of enterohepatic cycling and bile lipid composition are related to the speed of gallbladder emptying postprandially[30,31]. As bile is most lithogenic during fasting[2] the rate of emptying in the interdigestive period is probably more critical in the pathogenesis of gallstones. Supersaturation of bile is not solely sufficient cause for cholesterol cholelithiasis[3]; abnormal interdigestive gallbladder motility may well provide the link between hepatic secretion of supersaturated bile and lithogenesis.

References

1. Admirand WH, Small DM. The physicochemical basis of cholesterol gallstone formation in man. *J Clin Invest* 1968: **47**: 1043–52.
2. Metzger AL, Adler R, Heymsfield S, Grundy SM. Diurnal variation in biliary lipid composition: possible role in cholesterol gallstone formation. *N Engl J Med* 1973; **288**: 333–6.
3. Holzbach RT, Marsh M, Olszewski M, Holan K. Cholesterol solubility of bile, evidence that supersaturated bile is frequent in healthy man. *J Clin Invest* 1973; **52**: 1467–79.
4. Hepner GW. Effect of decreased gallbladder stimulation on enterohepatic cycling and kinetics of bile acids. *Gastroenterology* 1975; **68**: 1574–81.
5. DiMagno EP, Hendricks JC, Go VLW, Dozois RR. Relationships among canine fasting pancreatic and biliary secretions, pancreatic duct pressure, and duodenal phase III motor activity—Boldyreff revisited. *Dig Dis Sci* 1979; **24**: 689–93.
6. Keane FB, DiMagno EP, Dozois RR, Go VLW. Relationships among canine interdigestive exocrine pancreatic and biliary flow, duodenal motor activity, plasma pancreatic polypeptide, and motilin. *Gastroenterology* 1980; **78**: 310–6.
7. Itoh Z, Takahashi I. Periodic contractions of the canine gallbladder during the interdigestive state. *Am J Physiol* 1981; **240**: G183–9.
8. Traynor OJ, Dozois RR, DiMagno EP. Canine interdigestive and postprandial gallbladder motility and emptying. *Am J Physiol* 1984; **246**: G426–32.
9. Scott RB, Strasberg SM, El-Sharkawy TY, Diamant NE. Regulation of the fasting enterohepatic circulation of bile acids by the migrating myoelectric complex in dogs. *J Clin Invest* 1983; **71**: 644–54.
10. Peeters TL, Vantrappen G, Janssens J. Bile acid output and the interdigestive migrating motor complex in normals and in cholecystectomy patients. *Gastroenterology* 1980; **79**: 678–81.

11. Scott RB, Strasberg SM, El-Sharkaway TY, Diamant NE. Fasting canine biliary secretion and the sphincter of Oddi. *Gastroenterology* 1984; **87**: 793–804.
12. Torsoli A, Corazziari E, Habib FI, Biliotti D, Primerano L, Giubilei D. Prolonged recording of basal sphincter of Oddi activity. *Gastroenterology* 1985; **88**: 1616.
13. Toouli J, Dent J, Bushell M, Wycherly A, Stevenson G, Iannos J. Gallbladder emptying in relation to duodenal interdigestive migrating motor contractions. *Gastroenterology* 1985; **88**: 1616.
14. Kraglund K, Hjermind J, Jensen FT, Stodkilde-Jorgensen H, Oster-Jorgensen E, Pedersen SA. Gallbladder emptying and gastrointestinal cyclic motor activity in humans. *Scand J Gastroenterol* 1984; **19**: 990–4.
15. Doyle JS, Farrar JT. A sphincter mechanism in the cystic duct of dogs. *Ir J Med Sc* 1969; **2**: 109–17.
16. Code CF, Marlett JA. The interdigestive myo-electric complex of the stomach and small bowel of dogs. *J Physiol* 1975; **246**: 289–300.
17. Arndorfer RC, Stef JJ, Dodds WJ, Linehan JH, Hogan WJ. Improved infusion system for intraluminal esophageal manometry. *Gastroenterology* 1977; **73**: 23–7.
18. Sheltawy MJ, Losowsky MS. Determination of faecal bile acids by an enzymatic method. *Clinica Chimica Acta* 1975; **64**: 127–32.
19. O'Brien JJ, Shaffer EA, Williams LF, Small DM, Lynn J, Wittenberg J. A physiological model to study gallbladder function in primates. *Gastroenterology* 1974; **67**: 119–25.
20. Almond HR, Vlahcevic R, Bell CG, Gregory DH, Swell L. Bile acid pools, kinetics and biliary lipid composition before and after cholecystectomy. *N Engl J Med* 1973; **289**: 1213–6.
21. Simmons F, Ross APJ, Bouchier IAD. Alterations in hepatic bile composition after cholecystectomy. *Gastroenterology* 1972; **63**: 466–71.
22. Shaffer EA, Braasch JW, Small DM. Bile composition at and after surgery in normal persons and patients with gallstones—influence of cholecystectomy. *N Engl J Med* 1972; **287**: 1317–22.
23. Ryan TD, Pellegrini CA, Way LW. Bile kinetics in the conscious dog. *Surgical Forum* 1983; **34**: 234–6.
24. Takahashi I, Kern MK, Doods WJ *et al.* Contractile pattern of opossum gallbladder during fasting and after feeding. *Am J Physiol* 1986; **250**: G227–35.
25. Owyang C, Achem-Karam SR, Vinik A. Pancreatic polypeptide and intestinal migrating motor complex in humans: Effect of pancreaticobiliary secretion. *Gastroenterology* 1983; **84**: 10–17.
26. Scott GW, Otto WJ. Resistance and sphincter-like properties of the cystic duct. *Surg Gynecol Obstet* 1979; **149**: 177–82.
27. Itoh Z, Takahashi I, Nakaya M, Suzuki T. Arai H, Wakabayashi K. Interdigestive gallbladder bile concentration in relation to periodic contraction of gallbladder in the dog. *Gastroenterology* 1982; **83**: 645–51.
28. LaMorte WW, Schoetz DJ, Birkett DH, Williams LF. The role of the gallbladder in the pathogenesis of cholesterol gallstones. *Gastroenterology* 1979; **77**: 580–92.
29. Mok HYI, Von Bergmann K, Grundy SM. Kinetics of the enterohepatic circulation during fasting: biliary lipid secretion and gallbladder storage. *Gastroenterology* 1980; **78**: 1023–33.
30. Duane WC, Hanson KC. Role of gallbladder emptying and small bowel transit in regulation of bile acid pool size in man. *J Lab Clin Med.* 1978; **92**: 858–82.
31. Pomeranz IS, Shaffer EA. Abnormal gallbladder emptying in a subgroup of patients with gallstones. *Gastroenterology* 1985; **88**: 787–91.

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Raised serum thyrotrophin in women with peripheral arterial disease

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Women with symptomatic peripheral arterial disease were screened for impaired thyroid function using a sensitive immunoradiometric assay for thyrotrophin (TSH). The arterial disease in the aortotibial segment was documented by an abnormal brachial/ankle pressure index in 80 patients. An age-matched control group of elderly women ($n=30$) *with a normal pressure index was established. In the control group the mean serum TSH was 1·6 ± 1·1 milliunits/l, median 1·5 milliunits/l and this established a normal range of 0·2–3·9 milliunits/l. Seven patients (8·8 per cent) were already receiving treatment for myxoedema. In the remaining patients, the overall distribution of serum TSH was skewed to higher levels; the mean was 3·7 milliunits/l, median 2·4 milliunits/l,* $P<0{\cdot}001$ *compared with controls and 15 (19 per cent) had a serum TSH >4 milliunits/l, compared with only one (3·3 per cent) of the controls. Therefore 22 patients (28 per cent) had myxoedema or a raised serum TSH. For all subjects with a normal TSH, there was a positive correlation of serum TSH with serum cholesterol,* $r=0{\cdot}68$, $P<0{\cdot}001$. *For patients with a raised TSH, there was a continuing, but non-linear, increase of serum cholesterol with TSH. These results suggest that a raised serum TSH may be one of the risk factors for the development of peripheral arterial disease in women, possibly by increasing cholesterol levels.*

Keywords: Arterial disease, thyrotrophin, cholesterol

Hypercholesterolaemia is an important risk factor for coronary artery disease[1,2]. Auto-immune thyroiditis has also been considered to be a risk factor for coronary artery disease in women[3–6]. The association of minimal impairment of thyroid function and hypercholesterolaemia is controversial[7–12]. If auto-immune thyroiditis is causally related to arterial disease, this is more likely to be seen in women than men because the preponderance of men over women with degenerative arterial disease is matched by the reverse ratio of women to men with auto-immune thyroiditis. Peripheral arterial disease is often associated with coronary artery disease[13] but, unlike coronary artery disease, few workers have studied its association with auto-immune thyroiditis[14]. We have therefore measured total cholesterol and thyrotrophin (TSH) levels in patients with peripheral arterial disease and in controls, using a sensitive immunoradiometric method of measuring TSH.

Patients and methods

The patient group consisted of 80 women consecutively attending the arterial clinic with presenting symptoms of claudication or rest pain. Most of these patients had an abnormal resting brachial/ankle pressure index and the remainder had an abnormal pressure index after exercising for 1 min[15]. A single patient had been inappropriately prescribed carbimazole; no others were taking medications known to interfere with thyroid function, e.g. amiodarone or fenclofenac but seven patients were receiving thyroxine supplement for myxoedema. There had been no recent radiological investigations with contrast media. A fasting blood sample was taken for the determination of smoking markers (carboxyhaemoglobin and thiocyanate), lipids, glucose and TSH.

The control group consisted of 30 women who were hospital voluntary workers or participating as controls in a study of the role of lipids in femoropopliteal bypass patency. This group all had a normal 1-min exercise test. A single clotted fasting blood sample was taken for the determination of lipids, TSH and thiocyanate. Some of the control subjects may have had significant arterial disease in other strategic sites (e.g. coronary or carotid arteries) but this was not assessed. None were known diabetics or receiving treatment for myxoedema.

The TSH was measured by an immunoradiometric assay using antisera purchased from Serono Diagnostics (Woking, UK) and Bioclin (Cardiff, UK). The between assay coefficient of variation was 6·3 per cent at a level of 1·2 milliunits/l. The assay was standardized against the second international reference preparation of TSH (MRC 80/558) and the lower detection limit was 0·2 milliunits/l, where the coefficient of variation was 28 per cent. Statistical analysis was performed using a statistics package on a Sirius-Victor computer. Cholesterol values were compared using the *t* test. The distribution of TSH in patients was non-parametric and was not linearized by logarithmic transformation. These results were analysed by the Mann–Whitney *U*-test. In the text, cholesterol levels and ages are given as mean ± s.d., TSH levels are given as mean ± s.d., median (range). The skewness was estimated, zero skewness being parametric and increasing positive skewness representing data skewed to the right of median.

Results

The mean age of the women with peripheral arterial disease was 70·5 ± 8·8 years which was not significantly different from that of the controls, 68 ± 7·2 years. Amongst the patients, four had diabetes mellitus and a further five had been found to have fasting blood glucose levels of 8–14 mmol/l since their first attendance at the arterial clinic. Estimation of smoking markers (carboxyhaemoglobin and thiocyanate) showed that 47 patients (59 per cent) were current smokers. Of the controls, five (17 per cent) admitted to smoking and this was confirmed by thiocyanate determination.

In the control group the mean TSH was 1·6 ± 1·1, median 1·5 (0·2–4·1) milliunits/l, skewness 1·05, thereby giving the upper limit of normal TSH as 3·9 milliunits/l (mean ±2 s.d.). In the patients, the TSH was significantly higher, mean 3·7, median 2·4 (0·9–27) milliunits/l, skewness 3·6, $P<0{\cdot}001$ (*Figure 1*). A single control subject had a TSH in excess of 3·9 milliunits/l. This woman with a TSH of 4·1 milliunits/l had an elevated

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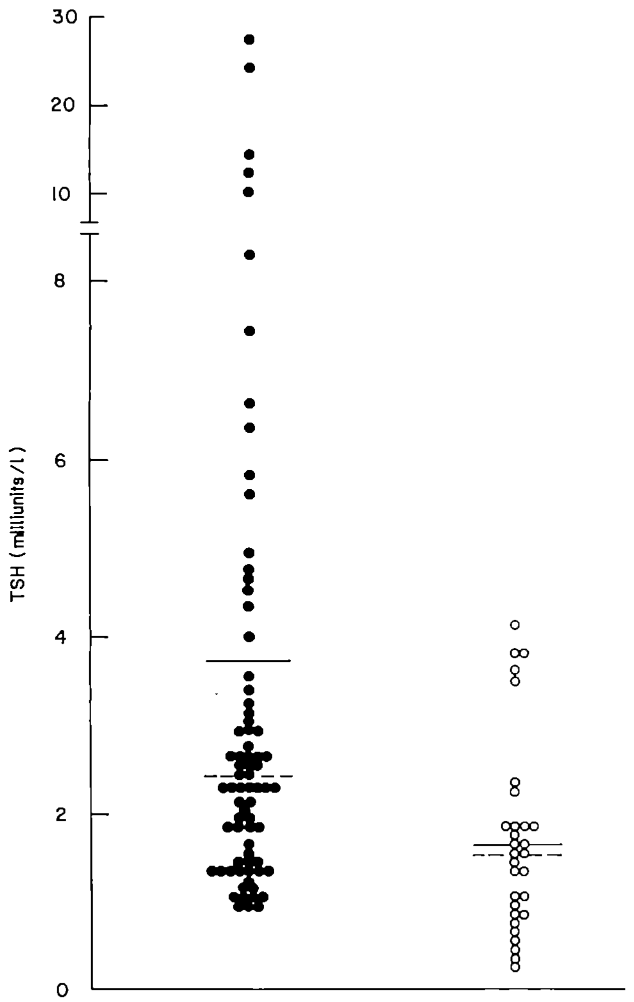

Figure 1 *Serum thyrotrophin in patients with peripheral arterial disease* (●) *and controls* (○). *Mean TSH* (——) *and median TSH* (– – –) *values are shown. The TSH values in patients are significantly higher than in controls,* $P<0\cdot001$

cholesterol (10·5 mmol/l), positive serum thyroglobulin antibodies and within 2 months of participation in this study had suffered a myocardial infarction. The serum thyroxine was lower in the patients (87 ± 19 nmol/l) than in the controls 97 ± 25 nmol/l), $P<0\cdot05$. There was no difference in serum thyroxine levels between patients with a TSH above or below 4 milliunits/l. There was no significant difference between the serum tri-iodothyronine in the patients (1·9 ± 0·3 nmol/l) and the controls (1·8 ± 0·3 nmol/l).

Of the 80 patients with peripheral arterial disease, 7 had myxoedema and were taking L-thyroxine. One patient who was taking carbimazole inappropriately and a further 15 (19 per cent) had a serum TSH in excess of 4 milliunits/l. Thyroid antibodies were present in the serum of 9 out of the 15 patients (60 per cent) with an elevated TSH compared with 2 of the 30 controls (χ^2, $P<0\cdot001$). Of the 58 patients with TSH <4 milliunits/l, 70 per cent were continuing smokers compared with only 33 per cent of the patients with a TSH above this range (χ^2, $P<0\cdot01$). There was no significant difference in the distribution of diabetics among patients with TSH <4 milliunits/l (7 out of 57) compared with those patients with TSH >4 milliunits/l (2 out of 15).

Within the normal range of TSH (0·2–4·0 milliunits/l) there was a positive correlation of TSH and serum cholesterol; the pooled data from controls and patients are shown in *Figure 2*, $r=0\cdot68$, $P<0\cdot001$. When the TSH ranges were fractionated it was evident that cholesterol levels were also significantly increased at high TSH levels (*Table 1*). The serum cholesterol of the total patient group, 7·0 ± 1·3 mmol/l, was higher than that observed in the controls, 6·3 ± 1·0 mmol/l, $P<0\cdot1$ (*Table 1*).

Discussion

Previous reports suggesting that hypothyroidism was not prevalent in hyperlipidaemia[16] or peripheral arterial disease[14] were probably the results of studies in a male-dominated group. The Whickham Study[9] showed that in males there was no association between an elevated TSH and hyperlipidaemia although there was a weak positive association in females. A positive association between hyperlipidaemia and minimal thyroid dysfunction has also been noted by Baschieri and co-workers[17]. In this study, use of the sensitive immunoradiometric assay for TSH, as an indicator of impaired thyroid function, has shown a marked difference in the prevalence of raised serum TSH in patients with symptomatic peripheral arterial disease compared with the control group. Two previous studies have reported on the prevalence of elevated serum levels of TSH or subclinical hypothyroidism in the general population; in the Whickham survey 10 per cent of women over 55 years had an elevated serum TSH[18] whilst in the United States an elevated serum TSH was found in 7·1 per cent of women over 60 years[19]. In our patients 8·8 per cent had myxoedema and 19 per cent had a raised serum TSH. Further, the median serum TSH of those not already taking thyroxine was much increased compared with controls.

The patient group in this study all presented with intermittent claudication. In the last decade the incidence of intermittent claudication in women aged 50–69 years was

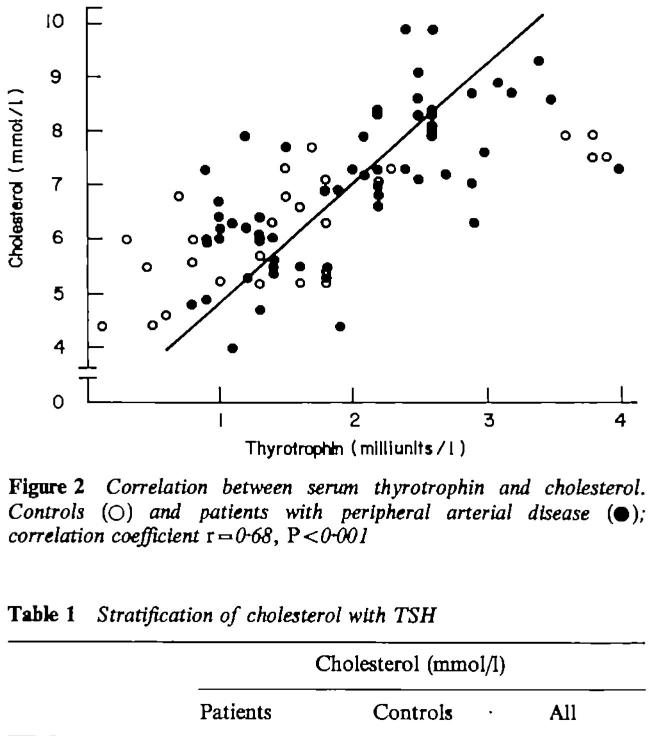

Figure 2 *Correlation between serum thyrotrophin and cholesterol. Controls* (○) *and patients with peripheral arterial disease* (●); *correlation coefficient* $r=0\cdot68$, $P<0\cdot001$

Table 1 *Stratification of cholesterol with TSH*

	Cholesterol (mmol/l)		
	Patients	Controls	All
TSH (milliunits/l)			
0–2	6·7 ± 1·2* (29)	6·1 ± 0·9 (23)	6·4 ± 1·1†
2–4	7·2 ± 1·4* (29)	6·8 ± 1·2 (6)	7·1 ± 1·4†
4–6	7·3 ± 0·7 (6)	—	
6–10	8·0 ± 0·8* (4)	—	
≥10	8·0 ± 0·6* (5)	—	
Thyroxine	6·2 ± 1·1 (7)	—	
Range	7·0 ± 1·3‡	6·3 ± 1·0‡	

Values in parentheses are the number of women studied

* Cholesterol at TSH ≥6 milliunits/l significantly higher than cholesterol at TSH 0–4 milliunits/l, $P<0\cdot01$

† Cholesterol at TSH 2–4 milliunits/l significantly higher than cholesterol at TSH 0–2 milliunits/l, $P<0\cdot01$

‡ Cholesterol of patient group ($n=80$) was higher than that in the controls ($n=30$), $P<0\cdot1$

1·2 per cent[20]. Therefore, we are observing a fairly common metabolic disturbance (raised serum TSH) in a group of patients with a less common complaint.

Although the mean serum thyroxine of patients was lower than the serum thyroxine of the controls, we have focused on the serum TSH as being the most reliable laboratory index of thyroid function. A recent study has shown that of the five analytes used in assessing thyroid function (total thyroxine, free thyroxine, total tri-iodothyronine, free tri-iodothyronine and TSH) only the measurement of TSH meets analytical goals[21] and that conventional population-based reference ranges for the other analytes may not be appropriate, especially for total thyroxine, where there is a high degree of individual variation[21].

Smoking is an established risk factor for peripheral arterial disease[22]. Smoking may alter serum lipids[23] and has been reported to reduce serum TSH levels[24,25]. Most patients (70 per cent) with TSH in the normal range were continuing smokers. Only 33 per cent of the patients with a TSH above 4 milliunits/l were continuing smokers compared with 17 per cent of controls (χ^2 insignificant). Borderline hypothyroidism, expressed as a raised serum TSH, appears to be an independent risk factor from smoking for peripheral arterial disease in women. The relationship of hypothyroidism to altered lipid metabolism is a subject of controversy[6–11], but the relationship of cholesterol with cardiovascular mortality is clearly established[1]. Here we observed an increased serum cholesterol, 8·0 ± 0·7 mmol/l, when the TSH was greater than 6 milliunits/l, and this could aggravate the degenerative arterial disease, but we also noticed a positive correlation between serum cholesterol and TSH levels even within the normal TSH range (*Figure 2*). This suggests that even small increases in serum TSH could contribute to cardiovascular morbidity. Previous workers[4] demonstrated that in elderly women a minimal increase in serum TSH was related to an increased risk of coronary artery disease.

Approximately one-third of the peripheral arterial disease patients have coexistent coronary heart disease[26]. L-thyroxine replacement can aggravate anginal pain. Screening for impaired thyroid function with improved laboratory techniques therefore creates a problem regarding the management of patients with minimal thyroid abnormalities. From careful study of our patients with peripheral arterial disease and borderline hypothyroidism we hope to establish whether treatment with L-thyroxine can prevent acceleration of, or even reverse, the peripheral arterial disease.

References

1. Rose G, Shipley M. Plasma cholesterol concentration and death from coronary heart disease: 10 year results of the Whitehall Study. *Br Med J* 1986; **293**: 306–9.
2. Keys A, ed. *Coronary Heart Disease in Seven Countries*. AHA Monograph No. 29. New York: American Heart Association, 1970.
3. Bastenie PA, Vanhaelst L, Neve P. Coronary artery disease in hypothyroidism observations in pre-clinical myxoedema. *Lancet* 1967; **ii**: 1221–2.
4. Tieche M, Lupi GA, Gutzwiller F *et al.* Borderline low thyroid function and thyroid autoimmunity. Risk factors for coronary heart disease? *Br Heart J* 1981; **46**: 202–6.
5. Dean JW, Fowler PBS. Exaggerated responsiveness to thyrotrophin releasing hormone: a risk factor in women with coronary artery disease. *Br Med J* 1985; **290**: 1555–7.
6. Fowler PBS, Swale J. Premyxoedema and coronary heart disease. *Lancet* 1967; **i**: 1077–9.
7. Fowler PBS, Swale J, Andrews H. Hypercholesterolaemia in borderline hypothyroidism. *Lancet* 1970; **ii**: 488–91.
8. Nilsson G, Nordlander S, Levin K. Studies on sub-clinical hypothyroidism with special reference to serum lipid pattern. *Acta Med Scand* 1976; **200**: 63–7.
9. Tunbridge WMG, Evered DC,. Hall R *et al.* Lipid profiles and cardiovascular disease in the Whickham area with particular reference to thyroid failure. *Clin Endocrinol* 1977; **7**: 495–508.
10. Alaghband-Zadeh J, Carter GD, Daly JR *et al.* Association between exaggerated responsiveness to thyrotrophin-releasing hormone and hypercholesterolaemia. *Lancet* 1977; **ii**: 998–1000.
11. Kutty KM, Bryant DG, Farid NR. Serum lipids in hypothyroidism—a re-evaluation. *J Clin Endocrinol Metab* 1978; **46**: 55–60.
12. Raziel A, Rosenweig B, Botvinic V *et al.* The influence of thyroid function on serum lipid profile. *Atherosclerosis* 1982; **41**: 321–6.
13. DeBakey ME, Lawrie GM, Glaeser DH. Patterns of atherosclerosis and their surgical significance. *Ann Surg* 1985; **201**: 115–31.
14. Sister J, Greenhalgh RM. Autoimmune thyroiditis in peripheral arterial disease. *J Cardiovasc Surg* 1980; **21**: 449–50.
15. Laing SP, Greenhalgh RM. Standard exercise test to assess peripheral arterial disease. *Br Med J* 1980; **i**: 13–16.
16. Lewis B. Premyxoedema: entity or nonentity? *Proc R Soc Med* 1977; **70**: 583–4.
17. Baschieri L, Fellin R, Martino E *et al.* Pituitary-thyroid function in hyperlipoproteinemia. *Rev Fr Endocrinol Clin* 1975; **16**: 211–17.
18. Tunbridge WMG, Evered DC, Hall R *et al.* The spectrum of thyroid disease in a community: the Whickham Survey. *Clin Endocrinol* 1977; **7**: 481–93.
19. Sawin CT, Chopra D, Azizi F *et al.* The aging thyroid. Increased prevalence of elevated serum thyrotrophin levels in the elderly. *JAMA* 1979; **242**: 247–50.
20. Hughson WG, Mann JI, Garrod A. Intermittent claudication: prevalence and risk factors. *Br Med J* 1978; **i**: 1379–81.
21. Browning MCK, Ford RP, Calaghan, Fraser CG. Intra and interindividual biological variation of five analytes used in assessing thyroid function: implications for necessary standards of performance and the interpretation of results. *Clin Chem* 1986; **32**: 962–6.
22. Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: the Framingham Study. *Am J Cardiol* 1976; **38**: 46–51.
23. Topping DL, Dwyer T, Weller RA. Peripheral vascular disease in cigarette smokers and impaired hepatic metabolism of lipoprotein remnants. *Lancet* 1977; **i**: 1327–9.
24. Christensen SB, Ericsson V-B, Janzon L *et al.* Influence of cigarette smoking on goiter formation, thyroglobulin and thyroid hormone levels in women. *J Clin Endocrinol Metab* 1984; **58**: 615–18.
25. Eden S, Jagenburg R, Lindstedt G *et al.* Thyroregulatory changes associated with smoking in 70-year old men. *Clin Endocrinol* 1984; **21**: 605–6.
26. Greenhalgh RM, Laing SP, Ellis M *et al.* How can we detect early subclinical disease? In: Greenhalgh RM, Jamieson CW, Nicolaides AN, eds. *Vascular Surgery: Issues in Current Practice 1986*. London: Grune & Stratton, 1986: 57–74.

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Immediate return of nerve function following microsurgical repair

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Recent reports suggest that there may be immediate return of sensory and motor function after microsurgical repair of peripheral nerves[1,2]. A previous study has demonstrated the conduction of nerve impulses across the suture line of recently repaired nerves[2]. However, whether such impulses generate muscle motor units (MMU) or induce a muscle contraction is unknown. We tested the hypothesis that impulses transmitted across an immediately sutured nerve would result in muscle contraction and movement of the limb. Under pentobarbital anaesthesia, the sciatic nerve was exposed in 9 New Zealand white rabbits. Monopolar stimulating needle electrodes were inserted into the sciatic nerve adjacent to the sciatic notch, while recording electrodes were inserted 3 cm distally. A concentric electrode was inserted into the calf muscles and a tremor transducer was attached to the paw. Nerve conduction velocity (NCV), the presence or absence of MMU and tremor amplitude following nerve stimulation were recorded before and after nerve transection between the electrodes and following microsurgical nerve repair. Results (mean ± s.e.m.) are shown in the Table.

		NCV (m/s)	MMU present (% animals)	Tremor amplitude
Pre-transection	$n=9$	10·8 ± 0·5*	100%*	28·1 ± 5·6*
Post-transection	$n=9$	0·0 ± 0·0	0%	2·1 ± 0·8
Post-repair	$n=9$	6·8 ± 0·7*	55%†	11·5 ± 1·7*

* $P<0·01$, †$P<0·02$ *versus* post-transection

These data indicate that in the rabbit (1) nerve conduction occurs across the suture line of a freshly repaired nerve, (2) NCV is reduced following nerve repair, and (3) stimulation of the proximal nerve can result in muscle contraction and limb movement. We suggest that peroperative electrophysiological assessment may be useful in the immediate evaluation of nerve function following microsurgical repair.

1. Chow SP, Luk DK, Ngai Y, *et al.* Immediate return of sensation after digital nerve repair. *Aust N Z J Surg* 1980; **50**: 228–32.
2. Lynch G, Quinlan D. Jump function following nerve division. *Br J Plastic Surg* 1986; **39**: 364–6.

Doppler ultrasound in the assessment of the acute scrotum

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Many infarcted testicles are removed annually for torsion[1]. To attempt to reduce this the policy of exploring all doubtful cases accepts negative explorations for epididymitis. A prospective study to distinguish torsion from other scrotal pathologies using an 8 MHz Doppler ultrasound pencil probe is reported.

The testicular vascular anatomy provides a detectable directional transverse blood flow from epididymis to opposite border[2]. Torsion obstructs arterial input reducing flow; epididymitis increases flow due to acute inflammatory hyperaemia[3]. The contralateral testis acts as control. Sixty-three normal patients were examined (mean age 23·2, range 5–82): sixty-two had equal Doppler signals, demonstrating the normal testis may reliably act as a control.

Sixty-five patients presenting with acute scrotal pain were examined. The Doppler findings did not influence the decision to explore. Of 30 cases of epididymo-orchitis (mean age 33·7, range 16–80), 29 had augmented Doppler signal. Of 21 cases of torsion (mean age 17·7, range 7–27) 20 had reduced/absent Doppler signal. Of 14 other pathologies (mean age 16·2, range 2–35) none had reduced/absent Doppler signal.

This study shows that Doppler assessment reliably distinguishes torsion from other acute scrotal pathologies and we consider its use mandatory in assessing the acute scrotum.

1. Leading article, Castration by neglect. *Br Med J* 1972; **1**: 128.
2. Milleret R, Liaras H. Ultrasonic diagnosis and therapy of torsion of the testis. *J Chir* 1974; **107**: 35.
3. Pedersen JF, Holm HH, Hald T. Torsion of the testis diagnosed by ultrasound. *J Urol* 1972; **113**: 1, 66–8.

Tissue plasminogen activator: a dose ranging study in acute peripheral arterial ischaemia

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Low dose intra-arterial streptokinase (SK) is an established method of non-operative management in acute peripheral arterial ischaemia. Tissue plasminogen activator (t-PA) is a new fibrinolytic agent available by recombinant DNA technology which may have enhanced thrombolytic effects and yet be safer than SK.

A total of 28 patients with limb threatening arterial occlusions less than 1 month old received intra-arterial thrombolysis by the following regimes: low dose SK (five patients), t-PA 2·5 mg/h (five patients), t-PA 1 mg/h (seven patients), t-PA 0·5 mg/h (six patients) and t-PA 0·25 mg/h (five patients).

Nineteen patients (68 per cent) had limb salvage 1 month after thrombolysis, six (21 per cent) required amputations and three patients (11 per cent) died. The systemic fibrinolytic effects of t-PA were very variable but fibrinogenolysis was pronounced in 22 per cent and did not appear to be dose related. Haemorrhage occurred in seven (25 per cent) t-PA patients, three required blood transfusion. One patient died from a haemorrhagic stroke. The thrombolytic effects and complications of t-PA and SK were comparable. Thrombolysis occurred more quickly with t-PA (mean 22 h) than with SK (35 h).

T-PA has been shown to be an effective thrombolytic agent in peripheral arterial ischaemia at all doses studied. Side effects and complications were comparable with SK, but t-PA may have the advantage of speed of action.

Polyunsaturated fatty acid ingestion and peptic ulcer—evidence of a direct relationship

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The incidence and virulence of peptic ulcer disease has fallen in the Western hemisphere. During this period the consumption of polyunsaturated fatty acids has increased[1]. We have examined the effects of polyunsaturated fatty acid ingestion on gastric acid secretion, prostaglandin output and serum gastric concentration[2]. Nine healthy volunteers supplemented their diet with 1·5 g or 3 g of linoleic acid, for 14–21 days.

LA did not affect gastroduodenoscopic appearances, gastroduodenal histology, routine haematology nor serum and urinary biochemistry. Four subjects developed mild diarrhoea. Mean basal gastric acid output was 8·3 ± 1·6 (s.e.m.) mmol/h before LA and 7·2 ± 1·3

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(s.e.m.) mmol/h after LA ($P>0\cdot05$). Mean pentagastrin stimulated gastric acid output decreased from 35·2±3·5 to 30·1±2·8 mmol/h after LA ($P<0\cdot05$). There was a corresponding increase in mean serum gastrin concentration from 19·22±3·7 to 30·89±3·8 pg/ml ($P<0\cdot01$). The mean output of immunoreactive PGE in gastric juice was 498±110 (s.e.m.) ng/h before LA, increasing to 1230±475 ng/h after LA ($P<0\cdot05$). The mean output of the main metabolite of PGE—13, 14 dihydro-15-keto PGE$_2$—in gastric juice was 192±19 (s.e.m.) ng/h before LA, rising to 1335(±708) ng/h after LA ($P<0\cdot01$).

These data suggest an explanation for the observed relationship between dietary polyunsaturated fatty acid intake and peptic ulcer disease: polyunsaturated fatty acid ingestion modifies local gastric prostaglandin metabolism with secondary changes in acid secretion and gastrin output.

1. Sonnenberg A, Muller H, Fabio P. Birth-cohort analysis of peptic ulcer mortality in Europe. *J Chron Dis* 1985; **38**: 309–17.
2. Hollander D, Tarnawski A. Dietary essential fatty acids and the decline in peptic ulcer disease—a hypothesis. *Gut* 1986; **27**: 239–42.

The anticancer effect of intraluminal calcium: reduced bile acid excretion and cell proliferation

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Dietary supplementation with calcium reduces the incidence of colorectal tumours in rats[1] and decreases intestinal cell turnover in both man and animals[2]. However its exact mechanism of action is unclear. Male Sprague–Dawley rats ($n=80$) received either an 80 per cent mid-small-bowel resection (SBR) or jejunal transection with reanastomosis, and half of each group had calcium lactate 24 g/l added to their drinking water. Seven weeks postoperatively serum calcium and phosphate were measured, and faeces were collected for estimation of free bile acid levels. Colonic mucosa from controls was grown in organ culture for 18 h in three different concentrations of calcium with subsequent stathmokinetic estimation of crypt cell production rate (CCPR). There was no significant difference in serum calcium between the four groups, although serum phosphate was 15–21 per cent lower in animals receiving added calcium (2·50±0·29 *versus* 2·06±0·20 mmol/l: $P<0\cdot02$). Calcium reduced faecal bile acid levels by 53–62 per cent (1·76±0·44 *versus* 0·82±0·23 mg/g dry weight of faeces: $P<0\cdot001$; 2·74±0·24 *versus* 1·03±0·42: $P<0\cdot001$), but SBR increased them by 26–57 per cent ($P=$ n.s. – $<0\cdot001$). In organ culture calcium 2–4 mmol/l reduced colonic CCPR by 22–68 per cent (4·80 *versus* 1·56–2·75 cells/crypt per hour, $P<0\cdot0001$–$0\cdot02$). Intraluminal calcium has a direct antitropic effect on the large bowel mucosa as well as reducing colonic levels of potentially carcinogenic bile acids.

1. Appleton GVN, Davies PW, Bristol JB, Williamson RCN. Inhibition of intestinal carcinogenesis by dietary supplementation

The overall cumulative survival in patients who were oestrogen receptor negative (ER –) was significantly better than in those patients whose tumours expressed oestrogen receptors (ER +), which was most marked in the female group. The median survival in the ER + women was 18·5 weeks compared with 33 weeks in the ER – women (log rank test, $P<0\cdot001$). The median survival in men was 20 weeks for ER + patients and 22 weeks for ER –.

These studies show that the presence of oestrogen receptors in gastric carcinoma is an indicator of poor prognosis in women, and suggest that sex hormone manipulation in men may have a role in the treatment of gastric carcinoma.

A reappraisal of the value of radiotherapy in early breast cancer: current perspectives from the Kings/Cambridge (Cancer Research Campaign) trial

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The Kings/Cambridge (Cancer Research Campaign) trial which accrued 2800 patients treated by simple mastectomy and randomized to either radiotherapy or watch policy now has a median follow-up of 12·9 years. Further analysis of the trial has confirmed the reduction of the incidence of local recurrence by radiotherapy, ($\chi^2=129\cdot71$, $P=0\cdot001$).

Altogether, 1980 patients have survived beyond 5 years with a total follow-up ranging up to 15·5 years. Thirty-two per cent of this group have died; the survival in the radiotherapy group being significantly worse than that of the watch policy group, ($\chi^2=6\cdot09$, $P=0\cdot01$). Analysis of the factors contributing to the excess mortality has been performed. Excess deaths were due to other causes than breast cancer, predominantly cardiovascular disease and non-breast malignancy. This effect was only seen in the patients with left-sided tumours ($\chi^2=13\cdot02$, $P<0\cdot001$).

Radiotherapy is effective in delaying local recurrence at the expense of a higher risk of death which manifests itself only after several years. It is suggested that adjuvant radiotherapy is reserved for patients believed to be at high risk of local recurrence or whose expectations of long-term survival is limited.

A new experimental model for the *in vivo* study of human breast cancer differentiation

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PMC42 is a unique human breast carcinoma cell line that differentiates both morphologically and functionally *in vitro*[1] and is stimulated by prolactin and EGF. Previous efforts to transplant PMC42 cells from monolayer culture into nude mice have failed, but fibroblasts have recently been shown to stimulate other human breast cancer xenografts[2].

[redacted]

Ultrasound detection of axillary lymph node metastases in breast cancer

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Pre-operative knowledge of the lymph node status of women with breast cancer would be of use in management. Clinical assessment is unreliable. Recently ultrasound detection of nodes has been suggested[1]. We have evaluated ultrasound in this role.

Ultrasound examination of the axilla was performed on 124 consecutive women with T_1 or T_2 breast cancer before surgery. A Sono-Diagnost B7100 B-Scan machine with 7·5 MHz head was used. Clinical examination of the axilla for lymph nodes was performed 'blind' in 81 patients whilst in 43 the clinician was aware his results were being assessed. All patients had full axillary clearance as part of their treatment.

Fifty-three patients had one or more lymph node metastases in the surgical specimen. The sensitivity of clinical examination in detecting involved nodes was 39 per cent when conducted 'blind' and 53 per cent when the clinician knew the patient was in a study (overall 42 per cent). The sensitivity of ultrasound detection was 61 and 63 per cent respectively (overall 62 per cent; $\chi^2 = 4{\cdot}57$, $P < 0{\cdot}05$). Overall specificity of axillary ultrasound was 79 per cent.

We conclude that ultrasound of the axilla in patients with breast cancer may be a useful adjunct to clinical examination for pre-operative detection of involved nodes but we have found it less effective than reported previously.

1. Bruneton JN, Caramella E, Hery M, Aubanel D, Manzino JJ, Picard JL. Axillary lymph node metastasis in breast cancer: Preoperative detection with US. *Radiology* 1986; **158**: 325–6.

Premorphological changes in normal epithelium from cancer bearing breasts

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Human breast cancer can be bilateral or multifocal. This suggests generalized neoplastic transformation in breast epithelium. Malignant progression from normal epithelium to invasive cancer can be recognized by the intermediate stages of atypical hyperplasia and carcinoma *in situ*. These changes are associated with and may be preceded by altered metabolism reflected in enzymatic imbalance. Benign breast tissue can be distinguished from malignant breast tissue by an alteration in the activity of the key enzyme glucose-6-phosphate dehydrogenase (G6PD)[1]. The aim of this study was to test the hypothesis that altered cellular metabolism precedes morphological changes during malignant progression.

Three tissue types were studied: normal (benign) breast tissue, morphologically normal tissue from a cancer bearing breast and malignant breast tissue. Using cytochemical techniques G6PD activity was measured at 5 and 10 min incubation under atmospheres of oxygen and nitrogen.

Table *Numbers of tissue with G6PD activity*

Tissue types	Oxygen 5 min	Oxygen 10 min	Nitrogen 5 min	Nitrogen 10 min
Normal (benign) $n = 25$	0	4	6	14
Normal (cancer bearing breast) $n = 15$	2	8	10	14
Malignant $n = 35$	18	27	25	35

Malignant tissue differs significantly from normal (benign) tissue ($P < 0{\cdot}001$ Fisher's exact test). Normal tissue from a cancer bearing breast differs significantly from normal (benign) breast tissue ($P < 0{\cdot}05$ Fisher's exact test) and is similar to malignant tissue.

Abnormal metabolism occurs widely within a cancer bearing breast. This abnormal metabolism can be detected before morphological changes have taken place.

1. Smyth PPA, Barron ET, Tobbia I, O'Higgins NJ. Cytochemical investigations of glucose-6-phosphate dehydrogenase activity in rat mammary tissue. *Br J Exp Path* 1987; **68**: 45–52.

The effect of stimulators of viral release on the reverse transcriptase activity from monocytes of patients with breast cancer

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We have previously reported that cell-free culture medium of incubated monocytes from patients with breast cancer contains reverse transcriptase (RT) suggesting the presence of a retrovirus in these cells.

Dexamethasone and 5-azacytidine are known to cause the release of retroviruses from cells in culture.

Purified monocytes from peripheral blood from patients with breast cancer were incubated in Eagle's medium supplemented with 10 per cent fetal calf serum. Parallel cultures were set up with no stimulator; with 10^{-6}M dexamethasone; or 7 μg/ml 5-azacytidine. After 6 days' incubation the supernatant was centrifuged at 600*g* for 10 min, filtered through a 220 nm micropore filter, and centrifuged at 100 000*g* for 1 h. The pellet was resuspended in TNE buffer. RT was assayed using a standard method with a synthetic RNA template in the presence of Mn^{2+}. Aliquots of the pellet suspension were centrifuged over a sucrose density gradient. RT was assayed at the different densities across the gradient.

No activity was detected in the cultures without a stimulator. Activity was consistently present when dexamethasone was used ($4{\cdot}1 \pm 0{\cdot}3$ pmol dCTP incorporated) but was significantly ($P < 0{\cdot}00001$; Student's *t* test) higher in the presence of 5-azacytidine ($25{\cdot}3 \pm 0.6$ pmol dCTP incorporated).

The RT activity was found in the density band 1·16–1·24 g ml^{-1} which is consistent with its being associated with a viral particle.

This study clearly indicates that dexamethasone and 5-azacytidine stimulate the release of retroviral particles from monocytes of breast cancer patients and these particles have a density similar to those observed in other retroviruses. These observations strongly suggest the presence of a retrovirus in monocytes from patients with breast cancer.

The value of tumour immunostaining with monoclonal antibody HMFG-1 to predict response to endocrine therapy and survival in patients with advanced carcinoma of the breast

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The value of steroid hormone receptors for the management of advanced carcinoma of the breast is often limited by the lack of availability of fresh tissue. Differentiation antigens may be estimated on paraffin embedded fixed material by immunostaining, and the aim of this study was to determine whether staining with the monoclonal antibody raised to human milk fat globule (HMFG-1), could replace receptor measurements.

The indirect immunoperoxidase technique was used to stain formalin-fixed paraffin-embedded tumour samples from 168 patients. All received tamoxifen or ovarian ablation as first-line systemic therapy, and all were evaluable for response (UICC criteria); 167 had oestrogen (ER) and progesterone receptors (PR) estimated. HMFG staining was assessed as the percentage of tumour cells stained, and by the site of stain. The proportion of cells stained was highly correlated with both ER ($P < 0{\cdot}0001$) and PR ($P < 0{\cdot}0001$) and with response. When ⩾30 per cent cells stained, 53 of 69 (77 per cent) responded; when 10–29 per cent stained 17 of 38 (45 per cent) responded, and when ⩽9 per cent cells stained 16 of 61 (26 per cent) responded ($P < 0{\cdot}0001$. Percentage of cells stained related to overall survival ($P < 0{\cdot}0001$).

Cox's multiple regression analysis of 42 prospective variables found that PR was the most important predictor of survival ($P < 0{\cdot}001$), but that after PR the percentage of cells stained with HMFG-1 was the most important ($P < 0{\cdot}0001$). We conclude that immunostaining for HMFG-1 gives similar information to receptor status, and has the advantage that fixed archival tissue may be used.

Apocrine differentiation: relationship to receptor status: prognosis and hormonal response in breast cancer

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The importance of apocrine differentiation in breast carcinoma is unknown. A 15 000 molecular weight breast cyst protein (BCP 15) associated with well differentiated tumours, is a marker of apocrine change[1].

The production of BCP 15 by tumour explants grown in tissue culture has been measured as a method of quantifying apocrine differentiation in 117 women with breast carcinomas with a minimum of 5 years' follow-up.

BCP 15 was detected by radioimmunoassay in the media from 90 per cent tumours (range 0–2·075 ng/ml, mean 41 ng/ml). Protein secretion by the tumour explants has been correlated with age, tumour grade, menopausal status, T stage, nodal status, oestrogen receptor (E_2R) levels, prognosis and *in vivo* response to hormonal therapy. Statistical analysis was by the Mann–Whitney Wilcoxon Rank Test. Tumour secretion of BCP 15 was higher in E_2R positive tumours ($P \leqslant 0{\cdot}05$) but was not of prognostic value.

Hormonal response was assessable by UICC criteria in 33 women (6 partial response: 8 stasis: 19 progression). Objective responders had significantly higher tumour E_2R levels ($P = 0{\cdot}002$) but a lower BCP 15 secretion (mean = 8·67 ng/ml) compared with non-responders (mean = 49·0 ng/ml, $P = 0{\cdot}017$). Apocrine differentiation in breast cancer (as defined by high BCP 15 production) is a marker for those E_2R positive tumours which do not respond to therapy.

1. Silva JS, Cox CE, Wells SA *et al.* Biochemical correlates of morphologic differentiation in human breast cancer. *Surgery* 1982; 92: 443–9.

Evidence for increased bone resorption in non-metastatic breast cancer

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There is a discrepancy between the degree of hypercalcaemia and the extent of bone metastases in patients with breast cancer[1]. This suggests that hypercalcaemia may be caused by mechanisms in addition to direct neoplastic invasion of the skeleton. Such mechanisms may be humoral in nature and result in hypercalcaemia by increasing bone resorption distant from tumour sites or increasing renal tubular resorption of calcium. The aim of this study was to look for evidence of humoral-mediated bone resorption in patients presenting with non-metastatic breast cancer.

We studied 15 women (mean age 56 years) with breast cancer. None had clinical, biochemical or scintigraphic evidence of skeletal metastases. Calcium release from bone was assessed from the fasting urine calcium/creatinine ratio. Transiliac bone biopsies were obtained at the time of definitive breast surgery and analysed for evidence of bone formation and resorption. These data were compared with 23 patients with bone loss due to osteoporosis. Histology showed a significantly higher osteoclast bone surface in patients with breast cancer than in osteoporotics (0·76 ± 0·20 *versus* 0·30 ± 0·09 per cent trabecular surface; $P < 0{\cdot}05$ mean ± s.e.m., Mann–Whitney *U* test), whereas bone formation rates were significantly lower in the osteoporotics (0·035 ± 0·006 *versus* 0·022 ± 0·004 mm^3/mm^2/years; $P < 0{\cdot}002$). Thus, the net bone loss assessed by fasting calcinuria was similar in the two groups.

These data suggest that bone resorption is pathologically enhanced even in patients with early breast cancer, supporting the view that tumour products have metastatic effects at sites distal from the primary or any secondary tumour.

1. Ralston S, Fogelman I, Gardner MD *et al.* Hypercalcaemia of malignancy and metastatic bone disease: is there a causal link? *Lancet* 1982; ii: 903–5.

Renal transplant vascular resistance (RVR)—prediction of immediate function (IF)

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The management of cyclosporin A treated renal transplant patients is simplified by IF of the kidney. We have examined the value of RVR in predicting IF. The Carolina e.m.f. flowmeter was used to measure renal blood flow (RBF) in 34 renal transplant patients 5 and 40 min after revascularization. The kidney was weighed and RBF calculated in ml min^{-1} 100 g^{-1}. Mean arterial pressure (MAP) was recorded from the external iliac artery with a pressure transducer. RVR was calculated as (MAP/RBF × 100). Twenty-four per cent of patients had primary non-function (PNF), and required dialysis in the first week post-transplant. IF was associated with a significant fall in RVR in the first 40 min after revascularization.

Table *RVR (mmHg min^{-1} ml^{-1})*

	5 min	40 min
IF $n = 26$	65 ± 68	39 ± 22*
PNF $n = 8$	110 ± 73	83 ± 50†

Results are means ± s.d.
Wilcoxon matched pair signed rank test (two tail) *$P < 0{\cdot}002$, †n.s.

There was a difference in RVR between IF and PNF kidneys at 5 min ($P = 0{\cdot}08$) and at 40 min ($P < 0{\cdot}02$, Mann–Whitney *U* test—two tail). The considerable variability in RVR seen at 5 min represents the summation of many donor and recipient factors. However both a low RVR at 40 min and a fall in RVR between 5 and 40 min were significantly associated with IF. RVR could be a useful parameter in the evaluation of protocols for increasing IF.

Metabolic efficiency of intraportal islet autografts in the cynomolgus monkey predicts long-term graft function

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Qualitatively normal islet hormone responses have been restored by intraportal islet autotransplantation after total pancreatectomy in cynomolgus monkeys as demonstrated previously, but the long-term function of such grafts is unknown. We have assessed long-term islet graft function in ten cynomolgus monkeys after total pancreatectomy and subsequent intra-portal islet autografting. Intravenous glucose (IVGTT, 500 mg/kg) tolerance tests were carried out 6 weeks after transplantation, K values calculated, and insulin responses measured. Fasting plasma glucose was normal or near normal in all animals for the first 3 months after transplantation. At between 3 and 18 months persistent fasting hyperglycaemia developed in 7 animals, while 3 animals maintained fasting normoglycaemia at 13, 15 and 22 months (*Table*).

Animal number	IVGTT K value	2 min insulin* (milliunits/l)	Graft survival (days)
1	1·92	6	65†
2	2·04	21	453†
3	1·02	−6	34†
4	2·07	36	675
5	0·91	−10	32†
6	1·98	31	459
7	2·89	17	256†
8	1·24	5	119†
9	1·92	20	410
10	2·17	15	199†

* Change from fasting values; †day of first fasting hyperglycaemia

Graft survival correlated with both 2 min IVGTT insulin responses ($r_s = 0{\cdot}98$, $P < 0{\cdot}001$) and IVGTT K value ($r_s = 0{\cdot}66$, $P < 0{\cdot}025$). These results suggest that the metabolic efficiency of pancreatic islet autografts 6 weeks after transplantation predicts long-term graft function. The rate of failure of 7 of these grafts may relate to implantation of an inadequate islet mass for control of glucose homeostasis.

NDS 61, a new monoclonal antibody to the rat interleukin-2 receptor (IL-2 R) induces long-term allograft survival

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Monoclonal antibodies to the IL-2 R have been used as immunosuppressive agents in murine cardiac transplantation models with limited success. We developed a new monoclonal antibody to the

IL-2 R which produced long-term allograft survival in a fully allogeneic rat strain combination.

A heterotopic cardiac allograft model was used in the LEW (RT-1^{1}) to DA (RT-1^{a}) strain combination. Graft function was assessed by palpation, ECG and at laparotomy. Purified antibody was administered in doses of 100, 300 and $900\,\mu g\,kg^{-1}\,day^{-1}$ IP for 10 days. The $300\,\mu g\,kg^{-1}\,day^{-1}$ IP dose was also given for 3 and 30 days. Intravenous and intraperitoneal administration were compared at $300\,\mu g\,kg^{-1}\,day^{-1}$ for 10 days.

NDS 61 given at a dose of $300\,\mu g\,kg^{-1}\,day^{-1}$ IP or IV for 10 days ($n=12$) prolonged allograft survival to greater than 100 days in 67 per cent of animals; the remainder rejected their grafts between 12 and 27 days (untreated controls: graft survival 7–11 days ($n=10$)): $900\,\mu g\,kg^{-1}\,day^{-1}$ or 30 days antibody administration did not improve survival; $100\,\mu g\,kg^{-1}\,day^{-1}$ or 3 days antibody therapy were ineffective.

This is the first demonstration of long-term survival following short-term treatment with an IL-2 R antibody in a fully allogeneic allograft model.

Effects of T cell subset-specific monoclonal antibodies on murine cardiac allograft rejection

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Selective manipulation of different T cell subpopulations with monoclonal antibodies may eventually lead to more refined immunosuppression in clinical organ transplantation[1]. We have examined the ability of monoclonal antibodies directed against either murine T helper/inducer cells (anti-L3T4 antibody) or T cytotoxic/suppressor cells (anti-Lyt 2 antibody) to prolong the survival of fully vascularized cardiac allografts in the mouse. Treatment with anti-L3T4 antibody significantly delayed graft rejection in three different strain combinations. Indefinite graft survival (100 days) was induced in 50 per cent of hearts in the C57BL/10 to C3H/HE combination (untreated control, MST = 9·2 days); in 67 per cent of heart grafts in the Balb C to CBA combination (untreated control, MST = 8·5 days); and in 33 per cent of grafts in the C57BL/10 to DBA/2 strain combination (untreated control, MST = 29·2 days). In contrast, anti-Lyt 2 antibody treatment did not delay first-set allograft rejection in the strain combinations tested. Cytofluorographic analysis revealed substantial depletion of target cells in both the peripheral blood and splenic compartments following antibody therapy. These results suggest that the L3T4 positive cell subset plays an important role in the first-set rejection of whole organ allografts and that monoclonal antibodies directed against the human homologue to L3T4 (CD4) could prove useful in clinical transplantation.

1. Cosimi AB, Colvin RB, Burton RC *et al*. Use of monoclonal antibodies to T cell subsets for immunologic monitoring and treatment in recipients of renal allografts. *N Engl J Med* 1981; **305**: 308–14.

Cyclosporin A prolongs survival of renal allografts by sparing T suppressor cells

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The mechanism of induction and maintenance of tolerance to alloantigens by cyclosporin A (CyA) remains unclear. It has been suggested that it may block T-helper cell activation while sparing T-suppressor cells (Ts)[1]. We have examined the effect of CyA on two distinct subsets of Ts previously demonstrated in spleens of long-term surviving (LTS) DA rats bearing Lewis kidneys[2]. Both subsets are CD$_8$+ but one is cyclophosphamide-resistant (CY^R). Naive, irradiated (200 rad) DA rats were adoptively transfused with CD$_8$+CY^R cells harvested from spleens of syngeneic hosts bearing LTS Lewis kidneys. The cell donor animals were given a 10-day course of CyA (day 10 to day 1) and a single dose of CY (day 1) before cell transfer (day 0). Lewis kidneys transplanted into these DA animals went on to LTS (MST > 100 days). Third party grafts were rejected as were Lewis grafts transplanted into naive recipients that received cells with the irrelevant phenotype (CD$_4$+) from those same CyA treated cell donors (MST = 10 days). However, naive DA recipients receiving CD$_8$+Cy^S cells from CyA treated cell donors, and transplanted with a third party (WAG) kidney, went on to LTS (MST > 100 days). Thus, we have clearly demonstrated two separate subsets of Ts resistant to CyA. This resistance sheds light on the mechanism of action of CyA.

1. Kupiec-Weglinski JW, Filho MS, Strom TB, Tilney NL. Sparing of suppressor cells: A critical action of cyclosporine. *Transplantation* 1984; **38**: 97–101.
2. Hutchinson IV. Alloreactive suppressor T cells: *Transplantation* 1986; **41**: 547–55.

Renal transplant rejection: 3- or 5-day course of methylprednisolone?

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Anti-rejection therapy with intravenous methylprednisolone (MP) was evaluated by fine needle aspiration cytology monitoring of the first rejection episode in 45 cadaveric renal allograft recipients immunosuppressed with cyclosporin. The total corrected increment (TCI) at diagnosis of rejection was 4·4 ± 1·7 (mean ± s.d.). Following MP 0·5 g daily for 3 days, the TCI was < 2·5 in 25 patients (group A). It remained > 2·5 in 20 patients (group B) and these were randomized to receive either no further MP at this stage (group B1), or MP 0·5 g daily for a further 2 days (group B2).

Nine group B1 and ten group B2 patients required further anti-rejection therapy within 28 days of the first rejection episode. Maintenance therapy was supplemented with oral prednisolone in 15 group B patients and azathioprine was subsequently added in 9 of these patients. Three patients failed to gain stable renal function. There was no difference in clinical outcome between groups B1 and B2. Only four group A patients required oral prednisolone of which one also required azathioprine.

We suggest that a TCI > 2·5 after a 3-day course of MP predicts the patients with incompletely treated rejection and those likely to experience further rejection episodes. Five days' treatment with MP does not affect subsequent outcome.

Group (n)	A (25)	B1 (10)	B2 (10)	A *versus* B	B1 *versus* B2
Days to rejection	11·0 ± 8·9	8·5 ± 5·5	5·8 ± 0·9	n.s.†	n.s.†
TCI at diagnosis	4·1 ± 1·6	4·9 ± 1·8	4·6 ± 1·6	n.s.†	n.s.†
TCI after MP	1·0 + 0·4	4·0 ± 1·0	5·4 ± 2·8	$P < 0\cdot001$†	n.s.†
Further rejection	8	9	10	$P < 0\cdot001$*	n.s.*

(mean ± s.d.). * χ^2 test; † Mann–Whitney *U* test

This work has been presented in part at the British Transplantation Society April 1987.

The role of protective agents in cyclosporin nephrotoxicity

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Cyclosporin (CyA) nephrotoxicity may be caused by a vascular mechanism. Therefore, agents which protect the kidney against reperfusion injury may be beneficial. Male New Zealand white rabbits (2·5–3·0 kg) were subjected to right nephrectomy and contralateral renal ischaemia for 90 min. In all groups of animals CyA was given in a daily IV dose of 25 mg/kg starting on the day of operation. Protective agents investigated were: mannitol (2 ml/kg IV 10 min before clamping), allopurinol (25 mg/kg IV 10 min before clamping) and prostacycline-PGI2 ($500\,ng\,kg^{-1}\,min^{-1}$ IV over 10 min after clamp release).

Group	Control	Allopurinol	Mannitol	PGI2
Number of animals	10	11	10	9
Day 1 creatinine median/range (mmol/l)	0·55 (0·42–0·68)	0·28 $P < 0\cdot0005$ (0·12–0·38)	0·30 $P < 0\cdot001$ (0·16–0·49)	0·62 (n.s.) (0·50–0·71)
Day 4 creatinine median/range (mmol/l)	0·32 (0·15–1·03)	0·15 $P < 0\cdot005$ (0·09–0·24)	0·18 $P < 0\cdot05$ (0·10–0·35)	0·82 (n.s.) (0·48–1·64)

(Significant differences from control by Mann–Whitney *U* test)

Electron microscopy and histology 10 days after operation showed reduced tubular and glomerular injuries in the mannitol and allopurinol groups. No animals in these groups died of renal failure while three out of ten of the control animals and six out of nine rabbits in the PGI2 group died of renal failure.

This study suggests that protection against reperfusion injury by mannitol and allopurinol may be effective in improving renal function when the kidney is exposed to the combined effects of ischaemia and CyA nephrotoxicity. PGI2 is thought to be both cytoprotective and a renal vasodilator but it may fail to reverse established vascular injury in the ischaemic kidney.

Evaluation of the therapeutic use of radioactive monoclonal antibody C242 in transplanted murine mammary tumours

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The therapeutic role of monoclonal antibody C242 labelled with ^{131}I was investigated in transplanted murine mammary carcinomas.

Ten milligram fragments of mammary tumour from (PxPc) F$_1$ hybrid mice were implanted subcutaneously in four groups of 12 mice of the same strain. Each group was injected intravenously at days 12, 24, 36 and 48 (following tumour implantation) with 0·2 ml PBS, C242-^{131}I or ^{131}I. McAb C242 was injected in a dose of 15 μg/injection and when radiolabelled it was conjugated with 17 mBq of ^{131}I.

By day.60, all the mice in the groups injected with PBS, C242 and ^{131}I were dead. By contrast, 8 of the 12 mice in the group injected with C242-^{131}I were still alive and well. There was also a significant difference in tumour size between the mice injected with PBS, C242 and ^{131}I (mean = 6·9 cm^2) and those injected with C242-^{131}I (mean = 4·7 cm^2; $P < 0{\cdot}01$).

Therefore this study has shown a beneficial antitumour effect of radiolabelled C242 in improving both survival and decreasing tumour size.

Malnutrition adversely affects non-specific cellular immunity but not anti-tumour lymphocytotoxicity in patients with gastrointestinal cancer

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It has often been claimed that the relative immunodeficiency seen in tumour-bearing patients is attributable to malnutrition. This has important implications for treatment with lymphokine-activated killer (LAK) cells[1] whose activity is impaired in patients with advanced gastrointestinal (GI) cancer since impaired LAK activity might be restored by nutritional support. Fifty-two pre-operative patients with GI cancer were classified as being either normally nourished ($n = 32$), or malnourished ($n = 20$) if they had >15 per cent loss of recall body weight and/or a serum albumin ≤32 g/l and/or a serum transferrin ≤2 g/l. Simultaneously lymphocyte function tests were performed consisting of lymphocyte stimulation in response to concanavalin A (Stimulation Index), interleukin-2 (IL-2) production (units/ml), basal and activated natural killer (NK) cell activity and LAK cell activity against the NK resistant cell lines DAUDI and COLO 320 adenocarcinoma. Mean (±s.e.m.) results were as follows:

	Stimulation index	IL-2 production	NK (% cytotoxicity)		LAK (% cytotoxicity)	
			Basal	Activated	DAUDI	COLO 320
Non-malnourished (mean serum albumin 40·3±0·9 g/l)*	108·9 ±12†	80·3 ±17·7	32·6 ±3·2	66·3 ±3·3	27·9 ±3·1	22·2 ±2·6
Malnourished (mean serum albumin 31·8±1·5 g/l)	64·3 ±11·3	69·9 ±12·1	24·23 ±3·4	63·3 ±4·1	22·9 ±5·3	21·1 ±7·3

Non-malnourished *versus* malnourished *$t = 5{\cdot}18$, $P < 0{\cdot}001$, †$t = 2{\cdot}39$, $P < 0{\cdot}01$

Malnourished GI cancer patients have impaired lymphocyte proliferation but do not have significantly impaired anti-tumour lymphocytotoxicity. We conclude that there would be no immunological necessity for nutritional support during adoptive cellular immunotherapy in these patients.

1. Rosenberg SA, Lotze MT, Muul LM *et al.* A progress report on the treatment of 157 patients with advanced cancer using LAK cells and IL2 or high dose IL2 alone. *N Eng J Med* 1987; **316**: 889–97.

Fatty acid composition of erythrocyte membranes in rats undergoing chemical carcinogenesis with *N*-nitrosomethylurea

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Tumours release factors into the circulation which modify the fatty acid composition of erythrocyte membranes[1]. Gas liquid chromatography was used to determine the fatty acid content of erythrocyte membranes in 37 female Sprague–Dawley rats undergoing chemical carcinogenesis with *N*-nitrosomethylurea (NMU). The tumour group (15) and non-tumour group (15) received NMU and were killed at 16 and 7 weeks. The controls (7) received no carcinogen and were killed at 16 weeks.

The median saturation index (ratio of stearic to oleic acid) was 1·16 in the tumour group, 1·53 in the non-tumour group and 1·73 in the controls. The saturation index (SI) differed significantly between the tumour and non-tumour groups ($P < 0{\cdot}03$) and between the tumour and control groups ($P < 0{\cdot}001$) but not between the non-tumour and control groups. There was also a significant increase in linoleic acid ($P < 0{\cdot}05$) and arachidic acid ($P < 0{\cdot}04$) but not in palmitic, stearic or eicosadienoic acid.

This study demonstrates a fall in the SI of rat erythrocyte membranes with tumour development, which is mainly due to an increase in the unsaturated oleic acid. This causes a decrease in membrane rigidity which is characteristic of cancer cells.

1. Habib NA, Wood CB, Apostolov K *et al.* Reduction in the stearic to oleic acid ratio in human malignant liver neoplasms. *Cancer Prevention and Detection* 1984; 7: 527.

Intra-operative radioimmunodetection of gastrointestinal neoplasms

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The intensity of radiation from a small source varies inversely with the square of the distance from the centre of that source. Placement of a gamma detector within millimetres from a source in intra-operative radioimmunodetection (IORD) enables the surgeon to take maximum advantage of this fact[1]. To assess if subclinical tumour deposits could be picked up applying IORD, the following experiment was designed. Twenty-six patients with gastrointestinal neoplasms were injected with ^{125}I labelled monoclonal antibody (Mab B72·3 ($n = 21$) and Mab 17-IA ($n = 5$)) pre-operatively and scanned intra-operatively using a hand held gamma detector (Neoprobe Columbus, Ohio). The gamma detector used in this study is gas sterilizable, contains a 1 cm cadmium telluride crystal and has a counting time of 2 s. Scanning at operation takes 10–15 min. Both monoclonal antibodies were made to non-circulating cell surface antigens from human colorectal cancer. Of the 26 patients, additional tumour that could not be palpated or visualized by the operating surgeon was picked up with the gamma detector in 5 (19 per cent). Increased radioactivity (arbitrarily defined as a tumour to background tissue ratio of greater than 1·5) was observed in 76 per cent of all cancer deposits. The median tumour to background tissue ratio was 5·4:1 (range 1:1–36:1). The optimal interval between injection of monoclonal antibody and intra-operative scanning was 10–15 days in this study. No adverse reactions were observed. The extent of tumour spread from gastrointestinal neoplasms can be better assessed at operation by addition of intra-operative radioimmunodetection to the surgeon's time honoured senses of inspection and palpation.

1. Aitken DR, Hinkle GH, Thurston MO *et al.* A gamma detecting probe for radioimmune detection of CEA-producing tumours: Successful experimental use and clinical case report. *Dis Colon Rectum* 1984; **27**: 279–82.

Metastatic tumour growth at colonic anastomoses: facilitation by surgical trauma

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Tumour cells injected into the left ventricle of rats distribute in proportion to the cardiac output[1]. Some organs, e.g. the adrenals and bone, are favoured sites for metastases whereas the colon never develops deposits. Trauma enhances metastatic growth[2] and local recurrence following colorectal resection is not uncommon[3].

Colonic anastomoses were performed in Hooded Lister rats and left ventricular injection of 10^5 MC28 sarcoma cells administered to different groups of animals at intervals between 2 h and 14 days following anastomosis and 1 h to 4 days before anastomosis. Histological examination was performed 16 days after tumour injection.

Tumours grew at the anastomosis in 76 per cent of animals ($n=50$) when injected 2–8 days following anastomosis but no deposits occurred when injections followed anastomosis ($n=17$) ($\chi^2=19{\cdot}5$; 1 d.f.; $P<0{\cdot}001$).

Following intraventricular injection of 10^5 labelled tumour cells, 960 trapped in the entire colon with no resulting deposits, whereas 120 cells lodged in the 1·5 cm of colon bearing the anastomosis, and resulted in a mean of 3 tumour nodules per anastomosis—a probability that 1 in 40 tumour cells arriving at an anastomosis will produce a deposit.

Spillage of malignant cells into the enhanced environment created by an anastomosis may facilitate local recurrence of colorectal cancer.

1. Murphy P, Alexander P, Kirkham N, Fleming J, Taylor I. Patterns of spread of blood borne tumour. *Br J Surg* 1986; **73**: 829–34.
2. Alexander JJ, Altemeier WA. Susceptibility of injured tissues to haematogenous metastases: an experimental study. *Ann Surg* 1964; **159**: 933–44.
3. Phillips RKS, Hittinger R, Blesovsky L, Fry JS, Fielding LP. Local recurrence following curative surgery for large bowel cancer: 1 The overall picture. *Br J Surg* 1984; **71**: 12–16.

Viable intraluminal tumour cells and local/regional tumour recurrence in experimental colon cancer

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To determine if viable intraluminal tumour cells can leak through a clinically intact anastomosis and cause local/regional tumour recurrence in a colon cancer model, the following experiment was undertaken. Six-week-old male Wistar/Furth rats ($n=22$) had their descending colon divided and a *water-tight* anastomosis performed using a single layer of 8–10 interrupted sutures under ether anaesthesia. Viable tumour cells (single cell suspension of 5×10^6 cells from a poorly differentiated Wistar/Furth colon cancer cell line in 1 ml of phosphate buffered saline) were then introduced intraluminally 2 cm proximal to the anastomosis by injection through a cannula which had previously been passed per rectum. The threshold cell number of 100 per cent tumour take for this tumour line was 5×10^4 viable cells. To exclude the possibility of intraperitoneal contamination with tumour cells at operation, a group of rats ($n=4$) underwent laparotomy and sham anastomosis under the same experimental conditions. No rats died postoperatively. Three to five weeks following operation, all rats except the sham group had clinically obvious intraperitoneal tumour. Sacrifice at this time demonstrated ascites omental and peritoneal metastases with perianastomotic tumour recurrence. All anastomoses were patent and intact and had no evidence of intraluminal tumour growth. Histological section through the anastomoses demonstrated infiltration of all layers of bowel wall and pericolic fat with poorly differentiated tumour. Viable intraluminal tumour cells cause local/regional tumour recurrence by leakage through a clinically intact anastomosis and may be an important cause of local/regional tumour recurrence in human colon cancer.

Pre-operative balloon occlusion of the renal artery does not reduce the incidence of metastasis or increase survival after radical nephrectomy for $pT_{1\text{-}3}$, N_0, M_0 adenocarcinoma

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Pre-operative balloon occlusion of the renal artery may increase survival following radical nephrectomy for adenocarcinoma by reducing systemic dissemination of cancer cells during tumour mobilization[1]. This concept was investigated prospectively in a study of 47 consecutive patients with renal adenocarcinoma treated by radical nephrectomy. Twenty-three patients (Group A) had pre-operative balloon occlusion of the renal artery by a standard technique[2]. Eighteen of Group A had $pT_{1\text{-}3}$, N_0, M_0 tumours and their follow-up ranged from 10 to 84 months (mean 46 months). Twenty-four patients (Group B) did not undergo pre-operative arterial occlusion. Nineteen of Group B had $pT_{1\text{-}3}$, N_0, M_0 tumours and their follow-up ranged from 10 to 96 months (mean 56 months). The incidence of metastasis and deaths from metastasis occurring after nephrectomy in those patients with $pT_{1\text{-}3}$, N_0, M_0 cancer were:

		Mestasis occurring after surgery			Deaths occurring from metastasis after surgery*		
Total		<6 months	6–12 months	>1 year	<6 months	6–12 months	>1 year
Group A	18	1	1	2	0	2	2
Group B	19	1	1	2	0	3	1

* $P>0{\cdot}5$ for survival time analysed by log rank test

Five patients in each group had involved nodes or metastasis at surgery and their mean survival times were Group A: 9·5 months and Group B: 10·8 months ($P>0{\cdot}5$).

The present findings do not support the proposal that pre-operative arterial occlusion improves the survival of patients with $pT_{1\text{-}3}$, N_0, M_0 renal adenocarcinoma treated by radical nephrectomy by reducing tumour embolization during surgery.

1. Mee AD. Prognosis after radical nephrectomy for carcinoma: the influence of pre-operative arterial balloon occlusion. *Br J Urol* 1982; **54**: 201–3.
2. Marberger M, Gunther R, Mayer EJ, Wiestler M. A simple method for in situ preservation of the ischaemic kidney during renal surgery. *Invest Urol* 1976; **14**: 191–3.

Serum prostate specific antigen measurement in prostatic disease

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Prostate specific antigen (PSA) is a glycoprotein with a molecular weight of approximately 35 000. It is present in the cytoplasm of prostatic cells only. It can now be assayed in serum using a radioimmunoassay.

Two hundred and fifty men have had serum PSA measurements. Thirty 'normal' controls had a mean PSA level of 2·18 ng/ml (1·9–4·7 ng/ml). One hundred and twenty with benign prostatic hyperplasia had a mean PSA of 13·0 ng/ml (1·9–80·2 ng/ml). Thirty-eight men with localized prostatic cancer had mean levels of 59·4 ng/ml (1·9–374) and 62 with metastatic disease 314 ng/ml (range 2·0–3574). Eighty-three men undergoing hormonal manipulation, either by orchidectomy, LH-RH analogues or anti-androgens, have been studied longitudinally. Four patients showed no clinical response and in each case PSA levels contined to rise. In the remaining patients a clinical response was paralleled by a fall in serum PSA levels. Disease progression has occurred in 20 men, in 19 (95 per cent) progression was accompanied by an increasing serum PSA. Overall for metastatic disease PSA had a sensitivity of 95 per cent, compared with 60 per cent for prostatic acid phosphatase and 85 per cent for alkaline phosphatase.

It is concluded that serum PSA measurement is a sensitive marker for advanced prostatic cancer and useful in monitoring its treatment.

Enhanced perfusion scintigraphy in metastatic liver disease

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The hepatic perfusion index (HPI) may be of value in the detection of liver metastases[1]. Because certain vaso-active agents can alter the distribution of blood flow between normal and neoplastic tissue[2] their administration during liver scintigraphy may enhance the predictive value of the HPI.

The aim of this study was to investigate the effect of angiotensin II (A II) on the HPI in patients with established metastatic liver disease. Perfusion liver scintigraphy was performed in 20 patients with proven metastases using ^{99m}Tc labelled tin colloid. In 12 patients the HPI was measured on two occasions: once during an intravenous infusion of A II (2–12 ng/min) and once during infusion of normal saline. Blood pressure was monitored throughout and the A II infusion adjusted to maintain a rise in systolic pressure of 15–20 mmHg. A reference group of 14 patients with no demonstrable liver abnormality was used for comparison of baseline HPI. The results are shown in the Table.

	Reference group (14)	Metastases group (20)
HPI (mean ± s.e.m.)	0·41 ± 0·03	0·60 ± 0·04 $P<0{\cdot}001$ (unpaired t test)
	Metastases group (12) (saline infusion)	Metastases group (12) (A II infusion)
HPI (mean ± s.e.m.)	0·64 ± 0·06	0·72 ± 0·08 $P<0{\cdot}01$ (Wilcoxon paired rank test)

These results confirm the value of the HPI in the detection of hepatic metastases. Furthermore, A II infusion significantly enhanced the HPI in patients with metastases and this may have implications not only for diagnosis but also for regional chemotherapy.

1. Leveson SH, Wiggins PA, Giles GR, Parkin A, Robinson PJ. Deranged liver blood flow patterns in the detection of liver metastases. *Br J Surg* 1985; **72**: 128–30.
2. Sasaki Y, Imaoka S, Hasegawa Y *et al*. Changes in distribution of hepatic blood flow induced by intra-arterial infusion of Angiotensin II in human hepatic cancer. *Cancer* 1985; **55**: 311–16.

The modified *N*-nitrosoproline test: results suggest that intragastric nitrosation may play a part in gastric carcinogenesis

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The role of intragastric nitrosation in the pathogenesis of gastric cancer in precancerous conditions such as pernicious anaemia and after gastric surgery remains controversial[1]. We have used a modification of the independent *N*-nitrosoproline excretion test[2] omitting the large nitrate challenge used in the original test. After an overnight fast L-proline (500 mg) was administered orally to patients who had previously undergone Polya partial gastrectomy ($n=15$), vagotomy (with or without pyloroplasty) ($n=9$), pernicious anaemia patients ($n=11$) and age matched controls ($n=20$). Twenty-four hour urinary *N*-nitrosoproline (N-Pro) excretion was then measured as an indicator of intragastric endogenous nitrosation. Urinary N-Pro levels were significantly lower in controls (median 0·93 μg/24 h, range 0–4·86 μg/24 h) compared with Polya partial gastrectomy patients (2·62 μg/24 h, range 0·29–9·18 μg/24 h; $P=0{\cdot}003$) and postvagotomy patients (1·75 μg/24 h, range 1·1–9·1 μg/24 h; $P=0{\cdot}03$). In pernicious anaemia patients N-Pro levels were also higher (median 1·44 μg/24 h, range 0–9·15 μg/24 h) than in controls but just failed to reach statistical significance.

This study has confirmed that surgically induced achlorhydria may result in increased intragastric nitrosation, thus allowing the formation of potentially carcinogenic *N*-nitrosamines.

1. Hall CN, Kirkham JS, Northfield TC. Urinary *N*-nitrosoproline excretion: a further evaluation of the nitrosamine hypothesis of gastric carcinogenesis in precancerous conditions. *Gut* 1987; **28**: 216–20.
2. Ohshima H, Bartsch H. Quantitative estimation of endogenous nitrosation in humans by monitoring *N*-nitrosoproline excretion in the urine. *Cancer Res* 1981; **41**: 3658–62.

Specific coagulation factors stimulate metastasis in experimental cancer

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In an animal model, warfarin inhibits metastasis after intravenous injection of tumour cells. Reconstitution of coagulation with the coagulation factors inhibited by warfarin (II, VII, IX and X) enhanced metastasis significantly[1]. This study seeks to clarify the mechanism underlying these observations.

Five groups of F344 rats received 10^4 Mtln3 mammary carcinoma cells either alone (Group A) or in combination with Factors II, VII, IX and X (Group B). Factor VII (Group C) or the complex of Factors II, IX and X (Group D). (These factors cannot be given separately because of purification difficulties.) Bovine serum albumin (BSA) was administered to a fifth group (Group E) to exclude non-specific enhancement by injected proteins. Numbers of lung metastases were assessed after 17 days[2], and groups compared using the Mann–Whitney *U* test.

Metastasis was significantly enhanced ($P<0{\cdot}001$) in Groups B and D compared with controls, suggesting an effect of the II, IX, X complex. BSA and Factor VII had no significant effect (*Table*).

Group	Median metastasis per animal	
A, Controls	13	
B, Factors II, VII, IX, X	182	$P<0{\cdot}001$
C, Factor VII	11	n.s.
D, Factors II, IX, X	181	$P<0{\cdot}001$
E, BSA	23	n.s.

These findings could not be explained by full activation of the coagulation system with fibrin formation, because in further experiments an identical Group B, pretreated with the defibrinating agent arvin, showed equal enhancement of metastasis.

These results suggest that metastasis is enhanced by a component of the Factor II, IX, X complex, via mechanisms which do not require full activation of the coagulation system.

1. McCulloch P, George WD. Warfarin inhibition of metastasis: the role of anticoagulation. *Br J Surg* (in press).
2. Wexler H. Accurate identification of experimental pulmonary metastases. *J Natl Cancer Inst* 1966; **36**: 641–5.

Intra-operative pelvic cytology accurately predicts those at risk of developing local recurrence of colorectal cancer

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Much attention is currently being paid to the importance of lateral clearance during operation for colorectal cancer in order to prevent local pelvic recurrence. We have examined 50 patients using intra-operative cytology to detect residual pelvic disease and report the correlation between positive cytology and the incidence of local recurrence.

The first 25 patients were examined by imprint cytology of tumour bed biopsies which were then submitted for histological examination. The second 25 patients were studied by scrape cytology of the four quadrants of the pelvis and histology was considered positive if there was tumour present in the perirectal fat.

Eleven of the fifty patients had positive cytology. Two died in the immediate postoperative period; there were five local recurrences in the remainder at a median follow-up of 20 months. Of the 39 negative patients, 9 were considered positive on histological criteria, with 1 local recurrence. There were 4 local recurrences in the 30 patients negative on both criteria, a highly significant difference ($0{\cdot}5>P>0{\cdot}25$, χ^2 test).

We conclude that intra-operative cytology accurately predicts those at risk of developing local pelvic recurrence. It is more important to detect malignant disease remaining in the patient than that removed with the histological specimen.

Recombinant human gamma interferon and adherent cell depletion in the generation of LAK cells in gastrointestinal cancer

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Adoptive cellular immunotherapy with lymphokine (Interleukin 2, IL-2) activated killer (LAK) cells is an exciting new approach in patients with malignant disease. However, LAK cell cytotoxicity is impaired in patients with advanced gastrointestinal (GI) cancer[1] and means of increasing their cytotoxic efficacy are required. We have examined the effects of removal of adherent cells (AC) (possibly suppressive) and co-culture with recombinant human interferon gamma (rHuIFNγ) (possibly stimulatory) on IL-2 stimulated LAK cell generation in 12 control subjects and 13 GI cancer patients. The mean (±s.e.m.) percentage LAK cell cytotoxicity before and after depletion of AC from peripheral blood mononuclear cells was 25·2 ± 3·48 per cent and 30·4 ± 4·8 per cent respectively in control subjects ($t^*=1{\cdot}56$, P n.s.) and 22·6 ± 5·4 per cent and 36·9 ± 4·6 per cent respectively in GI cancer patients ($t^*=4{\cdot}07$, $P<0{\cdot}001$). However, the mean cell loss following AC depletion was 38 ± 2·2 per cent, thus providing fewer cells for therapy. When AC depleted and non-depleted lymphocytes were stimulated with both IL-2 and 200 μg/ml rHuIFNγ the mean (±s.e.m.) LAK cytotoxicity was as follows:

	Non-depleted		AC depleted	
	−rHuIFNγ	+rHuIFNγ	−rHuIFNγ	+rHuIFNγ
Controls ($n=8$)	31·9±5·9	33·5±9·8	30·5±6·4	30·0±6·7
GI cancer ($n=11$)	21·6±5·3[a]	32·8±8·3[b]	42·7±3·9[c]	36·3±4·3[d]

Results are percentages; a *versus* b, $t^*=2{\cdot}67$, $P<0{\cdot}02$, c *versus* d, $t^*=2{\cdot}32$, $P<0{\cdot}03$, *paired *t* test

Thus, although AC depletion does increase LAK activity in GI cancer patients, this results in a reduced cell yield for therapeutic purposes. Conversely, the addition of rHuIFNγ significantly augments LAK cell generation in non-depleted cells (but reduces it in AC depleted cells), suggesting the participation of another cell in LAK cytotoxicity and is thus the preferable procedure for therapeutic LAK cell generation.

1. Monson JRT, Ramsden CW, Giles GR, Brennan TG, Guillou PJ. Lymphokine-activated killer cell production in patients with gastrointestinal cancer. *Gut* 1986; **27**: A1257.

Microwave thermography in the diagnosis of acute appendicitis

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Microwave radiation can travel several centimetres through body tissues[1]. This allows internal tissue temperature to be measured at the skin surface by the new technique of microwave thermography (MWT). The technique may therefore have a role in the detection of inflammatory foci. This study examines the ability of MWT to detect sites of local inflammation within the abdomen.

Seventy-two patients with suspected appendicitis and 30 control subjects were studied. Transverse microwave scans were taken at 1 cm intervals across the lower abdomen. A positive scan was defined as one with a localized temperature rise of >0·5°C in the right iliac fossa.

Scans on the 30 normal subjects were all negative and showed symmetry across the abdomen. Of the 72 patients with suspected appendicitis 52 underwent operation: 38 had histologically proven appendicitis, 7 had other local pathology in the RIF and in 7 no abnormality was found. The remaining 20 patients were discharged within 24 h. Positive scans were recorded in 38 of the 45 patients with significant pathology (sensitivity 84 per cent) while negative scans were recorded in 19 of 27 patients with non-specific pain or negative operative findings (specificity 70 per cent).

MWT scan	Appendicitis	Other pathology	Negative operation	Non-operated group
Positive	31	7	3	5
Negative	7	0	4	15

These results suggest that MWT may be clinically useful in the detection of sites of local inflammation within the abdomen.

1. Land DV. A clinical microwave thermography system. *Proceedings Institute of Electrical Engineers* 1987; **134**: 193–200.

The role of vasopressin (aVP) in the regulation of haemostasis during surgical procedures

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Major abdominal surgery is associated with a high risk of thrombotic complications and activation of coagulation during surgery is important in this process. The mechanisms involved in mediating the changes in haemostasis are unclear, but we have shown that high physiological concentrations of the stress hormone aVP, comparable to those observed during operations, produce increases in factor VIII and in plasminogen activator activity (PAA).

To investigate the role of aVP, 7 patients undergoing laparotomy (bowel manipulation and tissue damage) and 12 patients undergoing colonoscopy (bowel manipulation without tissue damage) were studied before and during these procedures. Venous blood samples were taken for plasma aVP, FVIII coagulant activity (FVIIIC), PAA and fibrinopeptide A (FPA).

During laparotomy, median aVP increased from 0·8 to 51 pg/ml ($P<0{\cdot}005$), FVIIIC from 1·95 to 2·2 units/l ($P<0{\cdot}05$), PAA from 31 to 331 units ($P<0{\cdot}05$) and FPA from 5·2 to 56 pmol/ml ($P<0{\cdot}05$). During colonoscopy, aVP rose from 0·5 to 153 pg/ml ($P<0{\cdot}02$), FVIIIC from 1·0 to 2·2 units/l ($P<0{\cdot}02$), PAA from 20 to 179 units ($P<0{\cdot}01$), but FPA remained unchanged.

These findings suggest that endogenous aVP released in response to bowel manipulation primes the clotting and fibrinolytic mechanisms, but that tissue damage is necessary for activation of thrombin and the formation of fibrin. Anaesthetic techniques which avoid a stress response, such as epidural anaesthesia, may reduce thrombotic complications.

Ischaemic foot muscle metabolism investigated by ^{31}P-magnetic resonance spectroscopy

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^{31}Phosphorus magnetic resonance spectroscopy (^{31}P-MRS) is a non-invasive means of assessing tissue energy metabolism. We have used it to study quantifiable changes in foot muscle metabolism associated with peripheral vascular disease (PVD). Fourteen patients, with either rest pain or calf claudication due to PVD, and eight age-matched controls were studied. Five patients were re-studied following angioplasty or bypass surgery.

Resting ankle Doppler pressures (RAPs) were measured in all patients. Spectra were collected from the foot muscle extensor digitorum brevis using a 2·2 cm surface coil. Intracellular concentrations of phosphocreatine (PCr) and inorganic phosphate (Pi), the phosphorylation potential (a measure of energy yield from ATP breakdown) and pH were determined from the spectra.

	PCr (mM)	Pi (mM)	*Phos. pot.$^{-1}$	pH	RAP (mmHg)
Patients with	20·24	13·4*	198†	7·19	42
rest pain ($n=9$)	±6·99	±6·24	±189	±0·12	±30
Patients with	32·64	6·7	22	7·16	78
claudication ($n=5$)	±9·62	±1·8	±22	±0·08	±27
Controls ($n=8$)	29·74	6·0	25	7·11	>brachial
	±5·78	±2·3	±21	±0·04	

Significance of difference from controls (paired *t* test): $*P<0{\cdot}01$, $\dagger P<0{\cdot}05$. * The inverse of the phosphorylation potential is given.

Muscle ischaemia was associated with a high Pi concentration, low PCr concentration and low phosphorylation potential. Three patients had ischaemic ulceration; these had the most extreme metabolic changes. All patients reported an improvement in foot symptoms following surgery, and this coincided with significant metabolic improvement, but in only three did the RAP increase.

In this study the metabolic changes detected by MRS correlated better with the patient's symptoms and local tissue changes than did RAP. ^{31}P-MRS appears to offer a means of detecting and quantifying ischaemic changes in patients with PVD.

Infusion phlebitis: is it avoidable? A prospective clinical trial

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Infusion phlebitis is one of the commonest causes of postoperative morbidity. Despite this, the most effective means by which to avoid it remains unclear.

In this prospective trial 75 patients admitted for elective or emergency surgery were randomly allocated to one of three treatment groups. In Group A (control) intravenous lines were established in the operating theatre by an anaesthetist. In Group B the cannulas were resited on the first postoperative morning using a strict aseptic technique. In Group C the cannulas were resited using the same technique as in Group B but in addition 10 mg/l hydrocortisone was added to the infusates. Phlebitis was assessed twice daily.

The incidence of phlebitis in Group A was 60 per cent, significantly higher than in Groups B and C with 33 per cent and 36 per cent respectively (χ^2 test: $P<0·05$). Infusion site survival was longest in Group C. The addition of antibiotics to the infusions was associated with a higher incidence of phlebitis. The distribution within the groups of surgical disease, sepsis, age, sex, infusion fluid and additives was similar.

We conclude that meticulous attention to asepsis in cannula insertion technique is the most important factor in reducing the incidence of infusion phlebitis and that we should encourage anaesthetists to adopt in the anaesthetic room the methods of surgeons in the operating theatre.

Effect of hydroxyethyl rutosides on transcutaneous PO_2 measurements

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Hydroxyethyl rutosides have been shown to improve symptoms in patients with chronic venous insufficiency[1]. The present study was designed to test the hypothesis that by decreasing the amount of extravascular fluid in the lower limbs, Paroven (Zyma UK) might improve the cutaneous oxygen level without affecting venous return or blood flow. A controlled, randomized, double-blind protocol of Paroven (500 mg twice daily) against placebo tablets was used to study 49 patients with either lipodermatosclerosis or symptomatic varicose veins. All patients underwent clinical questioning and examination, arterial and venous Doppler assessment, bipedal ascending phlebography, foot volume studies using the water-filled plethysmograph and transcutaneous PO_2 (Radiometer, Copenhagen) measured on both legs and the right arm. Elastic stockings were not worn during the trial and the foot volume and transcutaneous PO_2 measurements were repeated after 4 weeks treatment. The results showed a significant improvement of both the absolute leg transcutaneous PO_2 from 63·44 to 66·97 mmHg ($P=0·05$) and the arm to leg ratio from 0·87 to 0·92 ($P=0·025$) in patients taking Paroven. The improvement of arm to leg ratio was most marked in patients with lipodermatosclerosis from 0·87 to 0·97 ($P=0·034$). In the placebo group transcutaneous PO_2 fell from 64·50 to 59·92 mmHg ($P=0·067$). This study supports the view that, in patients with lipodermatosclerosis who have a lowered transcutaneous PO_2, treatment with hydroxyethyl rutosides may be beneficial.

1. Pulvertaft TB. Paroven in the treatment of chronic venous insufficiency. *Practitioner* 1979; **223**: 838–41.

Inherent structural abnormalities of the long saphenous vein: a cause of femorodistal bypass graft failure?

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Early and late vein graft failure have been attributed to (i) endothelial cell damage at the time of vein harvesting and (ii) the development of intimal hyperplasia. The *in situ* technique has several theoretical advantages, i.e. preservation of an intact endothelial surface, possible reduced incidence of intimal hyperplasia, a more naturally compliant vessel wall and tapering.

A study was undertaken to assess the long saphenous vein in patients undergoing *in situ* femorodistal bypass graft (FD), (10M:3F, age range 36–80 years). Segments of the long saphenous vein were taken 10 cm below the knee, one before and one after stripping of the valves. A histological scoring system was used to quantify the degree of luminal stenosis (LS), intimal hyperplasia (IH), longitudinal muscle sclerosis (LMS) and circular muscle hypertrophy (CMH). LS was graded 1–4 (1 = 0–25 per cent, 2 = 26–50 per cent, 3 = 51–75 per cent, 4 = 76–100 per cent). IH, LMS and CMH were graded 1–4 according to the severity. Marked abnormalities were noted in all the long saphenous veins (*Table*).

Luminal stenosis Grade	IH Focal	IH Diffuse	LMS	CMH
FD 2·0+0·32	2·31+0·47	2·1+0·23	2·9+0·24	2·1+0·43

Results mean + s.e.m.

Endothelial cells were quantified before and after stripping with a Hall valvulotome. Post-stripping 25–100 per cent of the endothelial cells had been lost and replaced by a layer of fibrin.

These results suggest that early graft failure may occur as a result of a poorly endothelialized flow surface and the presence of intimal hyperplasia at the time of implantation. Marked degrees of muscle sclerosis and hypertrophy may explain the poor compliance of vein grafts and contribute to graft failure.

Femorodistal graft assessment: duplex scanning and ankle brachial pressure indices compared with angiography

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This prospective study examines the role of duplex scanning for graft assessment compared with ankle brachial pressure ratios (ABPR), judged against angiography.

In 48 patients (mean age 69; 35 men) 58 grafts (33 vein, 17 PTFE, 8 Dacron (C.R. Bard Inc., Massachusetts, USA)) were studied. Eighteen grafts were occluded. Duplex scanning detected all 40 patent grafts and incorrectly classified one occluded graft (sensitivity 100 per cent; specificity 94 per cent). An ABPR of 0·6 correctly classified only 33 grafts as patent (sensitivity 83 per cent; specificity 100 per cent).

Resting ABPR did not differentiate between normal limbs and those with localized, haemodynamically significant disease (P = n.s.: t test).

A simple stress test (ankle flexion for 2 min) improved differentiation for localized disease ($P<0·01$: t test). Receiver operator characteristic curve analysis demonstrated that duplex scanning was superior to both ABPR tests for detecting haemodynamically significant disease (sensitivity: resting ABPR 48 per cent; stress test ABPR 63 per cent; duplex 71 per cent).

Combining the information obtained from duplex scanning, resting pressures and the stress test a further improvement in detection of significant disease was found (sensitivity 87 per cent; specificity 94 per cent).

Pressure indices alone appear inadequate for graft assessment. When combined with duplex scanning haemodynamically significant disease can be detected, localized and intervention planned.

Comparison of platelet and endothelial cell function following cyclo-oxygenase inhibition

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Early return of endothelial function following cyclo-oxygenase inhibition may help prevent platelet deposition. In a randomized, controlled study, recovery of platelet and endothelial prostaglandin synthesis and function was compared in 54 New Zealand white rabbits after indobufen (3·5 mg/kg, $n=20$), aspirin (5 mg/kg, $n=24$) or 0·9 per cent saline (1 ml, $n=10$). Arterial prostacyclin (PGI_2) and platelet thromboxane A_2 (TXA_2) were measured by radioimmunoassay. Aggregation with arachidonic acid (1 mmol/l) was used to assess platelet function and endothelial function was measured by bioassay by its ability to prevent this reaction.

Time (h)	1	4	8	12	24
PGI_2 (ng/ml)					
Control	4·3±0·2	3·9±0·3	4·2±0·1	4·2±0·1	3·9±0·3
Aspirin	0·6±0·1	0·7±0·1	1·0±0·1	1·7±0·1	4·1±0·1
Indobufen	1·7±0·1	1·5±0·1	3·8±0·3	4·2±0·1	4·2±0·1
TXA_2 (ng/ml)					
Control	606±5	603±11	607±5	607±6	608±2
Aspirin	83±1	83±2	87±1	91±1	90±2
Indobufen	91±1	185±12	274±2	477±2	592±2
Aggregation (%)					
Control	93±7	87±10	84±6	81±8	86±11
Aspirin	16±4	12± 3	20±5	17±4	22±6
Indobufen	15±5	25± 6	33±8	72±6	81±13

Values are means ± s.e.m.

For up to 4 h, compared with control, both drugs inhibited PGI_2

($P<0{\cdot}005$), TXA_2 ($P<0{\cdot}005$) and platelet aggregation ($P<0{\cdot}01$) (paired *t* test). After indobufen PGI_2 levels and endothelial function recovered by 8 h, against 12 h for TXA_2 and platelet aggregation. After aspirin, while maintaining platelet inhibition, PGI_2 and endothelial function only recovered at 24 h.

We conclude that the earlier recovery of endothelial function after indobufen may benefit in limiting platelet deposition.

Antithrombin activity and transport during acute limb ischaemia

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Antithrombin (ATIII), a protein and major circulating anticoagulant, is reduced during limb ischaemia[1]. Hypercoagulability is the assumed cause, but increased transvascular protein movement secondary to altered microvascular permeability may play a role. In an intact canine hindlimb model we determined plasma fibrinogen levels, and ATIII activity in lymph and plasma, during 1 h of steady state (C), 6 or 8 h of arterial occlusion (I), and 3 or 1 h of reperfusion (R). Lymph-to-plasma total protein concentration ratio (L:P) was used as an index of transvascular protein movement. Four groups were studied: GI, sham operated ($n=5$); GII, moderate ischaemia ($n=7$); GIII, 6 h severe ischaemia ($n=7$); GIV, 8 h severe ischaemia ($n=5$). There was no change in parameters in GI or GII. Plasma ATIII was decreased during R in GIII, and throughout I and R in GIV. Lymph ATIII was decreased during severe ischaemia in both groups. Fibrinogen levels were reduced significantly throughout I and R in GIV.

	Steady state	Ischaemia	Reperfusion
GIII			
ATIII plasma (%)	92·1 ± 5·6	80·1 ± 8·8	73·1 ± 8·1**
ATIII lymph (%)	33·5 ± 6·6	6·4 ± 4·2*	33·7 ± 9·6
Fibrinogen (mg/dl)	218·0 ± 102·5	175·3 ± 46·1	218·4 ± 26·8
GIV			
ATIII plasma (%)	89·0 ± 4·6	53·6 ± 16·2**	52·8 ± 6·1**
ATIII lymph (%)	40·0 ± 3·9	15·5 ± 6·5**	13·0 ± 8·3*
Fibrinogen (mg/dl)	253·8 ± 39·0	201·2 ± 44·8**	195·6 ± 51·7**

All values are means + s.e.m. *$P<0{\cdot}01$, **$P<0{\cdot}005$

The reduction in lymph ATIII occurred, despite a progressive increase in L:P throughout I, 0·42 ± 0·02 to 0·64 ± 0·07 ($P<0{\cdot}001$) at 6 h in GIII and 0·46 ± 0·03 to 0·85 ± 0·2 ($P<0{\cdot}01$) at 8 h in GIV. Our data suggest that the reduction in antithrombin activity during limb ischaemia is not due to increased microvascular permeability to protein. The reduction in fibrinogen levels suggests that hypercoagulability may be implicated.

1. Miller SH, Eyster ME, Saleem A *et al.* Intravascular coagulation and fibrinolysis within primate extremities during tourniquet ischaemia. *Ann Surg* 1979; **190**: 227–30.

Plasma prostanoid levels and platelet function in Raynaud's syndrome and vibration white finger disease

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As abnormal prostanoid metabolism has been suggested as a factor in aetiology of vasospastic diseases we have measured prostanoid metabolite levels using a radio-immunoassay[1] in 13 patients with primary Raynaud's (RD), 10 with Raynaud's secondary to scleroderma (RP), 8 men with vibration white finger disease (VWF) and 25 normal subjects (N).

Table 1

	N	VWF	RD	RP
Plasma thromboxane B_2 level	7·6 ± 5·6	27·1 ± 28·3	15·0 ± 13·2	284 ± 9·0
Plasma 6-keto-PGF_{1a} level	0·76 ± 0·52	1·8 ± 2·0	0 98 ± 1·04	31·1 ± 16·5

Values are means ± s.e.m. in ng/ml

To determine if these abnormal levels are associated with disturbed platelet function, we have measured platelet aggregation[2] to ADP and collagen in the same patient groups. The extent of aggregation to low doses of ADP was the most discriminating parameter. The extent of aggregation to collagen (4 and 2 mg/l) did not distinguish between the groups. The duration of the collagen lag phase was reduced in both Raynaud's groups but prolonged in patients with VWF.

Table 2

	N	VWF	RD	RP
n	25	14	22	12
Extent of aggregation (%) to:				
2·50 μM ADP	55 ± 17	37 ± 17*	57 ± 15	59 ± 18
1·25 μM ADP	30 ± 22	17 ± 18*	41 ± 17*	55 ± 19*
0·625 μM ADP	5 ± 5	8 ± 18	23 ± 19*	26 ± 16*
Duration of lag phase (s) to:				
4 mg/l collagen	63 ± 20	91 ± 50	52 ± 28*	46 ± 26
2 mg/l collagen	90 ± 26	106 ± 63	77 ± 48*	86 ± 61*

(Values are mean ± s.e.m. *Mann–Whitney *U* test $P<0{\cdot}05$)

In patients with RP and RD platelet aggregability is enhanced, consistent with high thromboxane B_2 levels. Paradoxically, platelet aggregability is diminished in patients with VWF, despite the elevated thromboxane B_2 levels found in this group.

1. Wilkinson D, Vowden P, Latif AB, Rajah SM, Kester RC. The relationship between plasma eicosanoids and cold sensitivity. *Br J Surg* 1987; **74**: 328 (Abstract).
2. Born GVR. Aggregation of blood platelets by adenosine diphosphate and its reversal. *Nature* 1962; **194**: 927–9.

Free radical involvement in intermittent claudication

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Oxygen derived free radicals (O_2) are thought to mediate tissue damage in a number of conditions[1]. There is evidence that such damage is associated with alterations in vascular permeabiltiy and with micro-angiopathy in diabetics[2]. Diabetics with a generalized increase in vascular permeability show increased glomerular permeability to albumin leading to a small, but pathologically significant, increase in urinary albumin (micro-albuminuria)[3].

We set out to determine if O_2 reactions were implicated in patients with intermittent claudication, and whether this had a more generalized systemic effect manifest by a change in micro-albuminuria.

Nine non-diabetic patients with intermittent claudication, and nine healthy controls were exercised on a treadmill after a period of rest. Blood and urine samples were obtained before walking and during a 60 min recovery period. Lipid peroxides and diene conjugates, both products of O_2 activity, rose significantly in the claudicants after exercise compared with the controls ($P<0{\cdot}01$, Mann–Whitney *U* test). Urinary micro-albumins of the controls remained unaltered but rose significantly in the claudicants ($P<0{\cdot}05$, Mann–Whitney *U* test).

These results support the putative role of O_2 in ischaemia. This may have both diagnostic and therapeutic implications in patients with all stages of vascular disease.

1. Bulkey GB. The role of oxygen free radicals in human disease processes. *Surgery* 1983; **94**: 407–11.
2. Jennings PE, Jones AF, Florkski CM, Lunec J, Barnett AH. Increased diene conjugates in diabetic subjects with microangiopathy. *Diabetic Medicine* (in press).
3. Feldt-Rassmussen B. Increased transcapillary escape rate of albumin in type 1 (insulin dependent) diabetic patients with microalbuminuria. *Diabetologia* 1986; **29**: 282–6.

P_{tc,O_2} and the objective assessment of intermittent claudication

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Objective assessment of intermittent claudication remains difficult but important, if the numerous claims made for treatment benefit are to be substantiated. Many methods show great variability or fail to correlate with other indices of disease severity. Ankle systolic blood pressure after exercise is an accepted technique[1] but can be difficult to determine if the pressure decrease is large or the calf blood vessels are diseased and non-compliant.

We examined the role of transcutaneous oxygen tension (P_{tc,O_2}) measured on the dorsum of the foot in patients with claudication. P_{tc,O_2} has the advantage that it can be recorded continuously during walking and recovery. P_{tc,O_2} fell during exercise and returned to the previous level on stopping in subjects with claudication, but was unaltered in normals.

P_{tc,O_2} recovery time after exercise was recorded on 102 separate occasions and compared with ankle systolic pressure recovery times. There was a close correlation between these methods ($r=0{\cdot}86$, $P<0{\cdot}001$). In 25 patients the measurements were repeated after an interval of 1 week. Reproducibility, as determined by correlation of the values, was better for P_{tc,O_2} ($r=0{\cdot}91$, $P<0{\cdot}001$) than ankle pressure recovery time ($r=0{\cdot}84$, $P<0{\cdot}001$).

P_{tc,O_2} promises to be useful in the objective assessment of patients with intermittent claudication.

1. Sumner DS, Strandness DE. The relationship between calf blood flow and ankle systolic pressure in patients with intermittent claudication. *Surgery* 1969; **65**: 763–71.

Carotid endarterectomy: the influence of patch angioplasty and drugs on platelet deposition

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Acute thrombosis, intimal hyperplasia and restenosis may all result from platelet accumulation on the endarterectomized carotid[1]. We measured the duration of platelet deposition, the effect of platelet inhibitory therapy, and evaluated methods of arteriotomy closure.

Autologous ^{111}In-platelet uptake over 3 days was measured after unilateral carotid endarterectomy in 60 patients and compared with the contralateral artery as the carotid uptake ratio (CUR), with the daily increase in this ratio termed thrombogenicity index (TI).

Mean (±s.e.m.) CUR 3 days after surgery was 1·22±0·04 but returned to normal by 2 months at 1·01±0·06 ($P<0{\cdot}01$). Platelet inhibitory therapy significantly reduced CUR to 1·11±0·035 compared with 1·44±0·03 on no treatment ($P<0{\cdot}002$) with a similar reduction in TI to 0·06±0·02 from 0·34±0·07 ($P<0{\cdot}002$). CUR and TI were greater after patch angioplasty at 1·41±0·07 and 0·283±0·021, respectively, when compared with simple suture of the arteriotomy at 1·14±0·04 and 0·146±0·013 ($P<0{\cdot}01$). Vein and Dacron® patches accumulate platelets to the same degree with CURs of 1·47±0·17 and 1·37±0·07, respectively ($P>0{\cdot}5$).

Early platelet deposition is reduced by antiplatelet drugs but increased by patch repair of the artery. This platelet uptake, which may be important in restenosis and subsequent carotid occlusion, has largely ceased by 2 months, suggesting intimal repair.

1. Gallow AD, Recurrent stenosis after carotid endarterectomy. *Arch Surg* 1982; **117**: 1082–5.

Is atherosclerosis at the adductor canal related to exercise?

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Atherosclerosis is common at the adductor hiatus segment of the femoral artery where tendons are in close apposition to the vessel. Platelet–intimal interaction is associated with both arterial trauma and atherogenesis[1]. We have studied the effect of exercise on luminal platelet deposition in the femoral artery.

Autologous ^{111}In-labelled platelets were injected into 35 adult men. A total of 15 legs contralateral to an occluded femoral artery, 26 legs with generalized arterial stenoses and 14 disease free legs were studied. Femoral artery radioactivity was measured by gamma camera and probe counter on day 1 and, after a period of maximum tolerated exercise, on day 4. Luminal platelet deposition in each patent vessel by day 4 was expressed as the percentage change in the ratio radioactivity at the adductor hiatus (RA) to the radioactivity at the proximal femoral artery (RP).

	Femoral artery radioactivity		
	Unilateral femoral artery occlusion ($n=15$)	Generalized atherosclerosis ($n=26$)	Disease free ($n=14$)
Change RA/RP (%)			
Gamma camera	9·3±4·0*	3·6±1·6	−0·2±1·5
Probe counter	1·3±3·5	1·2±2·5	−6·4±4·6

All results are means±s.e.m. *$P<0{\cdot}02$ compared with disease free group (Mann–Whitney *U* test)

There is a significant increase in platelet accumulation after exercise over the adductor hiatus of arteries at risk, and this is not found in normal vessels. This may be related to the predisposition of the distal femoral artery to atherosclerosis.

1. Fishman JA, Ryan GB, Karnovsky MJ. Endothelial regeneration in the rat carotid artery and the significance of endothelial denudation in the pathogenesis of myointimal thickening. *Lab Invest* 1975; **32**: 339–51.

Pulsed Dye laser and atherosclerotic vascular disease

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The application of lasers in the treatment of peripheral vascular disease is now a clinical reality. However, the continuous wave lasers presently used are associated with thermal injury to the underlying vessel wall. Pulsed dye laser radiation (wavelength 504 nm, pulse length 1 μs, frequency 10 Hz) has been used to produce craters in human post-mortem aortic wall specimens. Laser power was 0·2–0·5 W (continuous wave equivalent), peak pulse power 50 kW. The energy was increased stepwise (2·5–10·0 J) and both normal and atheromatous tissue was vaporized.

Light and electron microscopic studies revealed minimal surrounding thermal effects. Radiation cut more deeply into atheromatous as compared with normal aortic wall, as measured by optical micrometry. The dose response in air for normal aorta was 10 μ/J and 85 μ/J in atheromatous aorta.

Energy (J)	2·5	5·0	7·5	10·0
Median and range crater depth (μm)				
Normal aorta	37 (20–90)	54 (25–90)	72 (45–230)	109 (60–300)
Atheromatous aorta	418 (375–590)	846 (725–902)	1128 (1070–1230)	1440 (1310–1530)

The crater depth was significantly greater in atheromatous tissue at all power levels ($P\leqslant 0{\cdot}01$, Mann–Whitney *U* test).

These results show that the pulsed dye laser demonstrates highly desirable effects on atherosclerotic tissue, which may be very relevant to the treatment of peripheral vascular disease.

Small diameter prostheses—tapered or straight?

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One advantage claimed for *in situ* vein bypasses is that they taper naturally, and so avoid the diameter mismatch at the distal anastomosis. This would improve the efficiency of flow energy transfer and avoid intimal hyperplasia[1,2].

We tested this theory by comparing a straight 6·5 mm diameter prosthesis (A) with one of similar material but only 5·0 mm diameter (B) and two tapered prostheses (C) and (D) 6·5–5·0 mm diameter. We calculated resistance to flow, impedance (resistance to pulsatile flow), energy transfer, the velocity of flow and pulse wave speed (PWS). Calculations were made for conditions simulating both a high and low peripheral resistance, 'bad' and 'good' run-off. For comparison values are normalized to those for tube (A).

			Mean velocity		Impedance		
	Resistance	PWS	'Good'	'Bad'	Proximal	Distal	Energy loss
A	100	100	100	100	100	100	0
B	286	89	59	169	151	151	0
C	173	94	75	130	78	193	0·05
D	252	90	60	151	69	280	0·13

The ideal tube would match the impedance of the arteries at both ends, i.e. show an impedance taper, high velocity of flow with minimum energy loss.

In conclusion, when peripheral resistance is high, tapered tubes have advantages over straight ones.

1. Klimach OI, Chapman BLW, Underwood CJ, Charlesworth D. An investigation into how the geometry of an end to side arterial anastomosis affects its function. *Br J Surg* 1984; **71**: 43–5.
2. Hasson JE, Megerman J, Abbott WM. Increased compliance near vascular anastomoses. *J Vasc Surg* 1985; **2**; 419–23.

A rationale for heating in toe-pressure measurements

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Although ischaemic tissue is, in theory, maximally vasodilated, this may not always be the case. There can be a significant degree of vasomotor tone which would adversely affect digital pressure assessment. We set out to examine the role of acral heating in such measurements. Digital pressure measurements were performed using photoplethysmography and 2-cm toe cuffs on 50 great toes, before and after vasodilation. There were 16 normal toes (ankle/brachial index >1·0), 17 toes with severe ischaemia (toe pressure <40 mmHg) and 17 toes with moderate ischaemia (toe pressure >40 mmHg and ankle/brachial index <1·0). Vasodilation was achieved by heating with an extrinsic source to 30°C, as measured by a skin thermocouple. Relative temperature and pressure increases were recorded and correlated with each other and with the extent of disease. There was a significant pressure rise in all patients ($t=13·2$, $P<0·001$, paired t test). This rise was most apparent in patients with moderately severe disease (±preheat = 70·5 mmHg, ±postheat = 90 mmHg) but not as obvious in normals (±preheat = 101 mmHg, ±postheat = 114·5 mmHg), while the change in severely ischaemic feet varied considerably (±preheat = 21 mmHg, ±postheat = 31·5 mmHg). This study shows that extrinsic heating is an essential component in toe pressure measurement. Moreover, some toes with apparent severe ischaemia need to be recategorized. Such a phenomenon may be of great significance in the further management of these patients. It is clear that toe pressure measurements should be standardized to prevent misleading interpretation of data and so allow meaningful comparative studies to be performed.

Effective endothelial cell adhesion to Dacron graft

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Inoculated endothelial cells may improve the performance of prosthetic vascular grafts[1]. We have examined the role of substrates to promote endothelial cell bonding to Dacron®, and assessed the effect of endothelial cell cover on platelet adhesion.

Human adult endothelial cells, labelled with ^{111}In-oxine, were inoculated on to prosthetic surfaces prepared with cold insoluble globulin (CIG), 1 per cent gelatin, alginate or untreated. At 100 min the surfaces were irrigated and the radioactivity in the effluent was measured. Mean percentage cell adhesion to CIG and 1 per cent gelatin was similar at 86·1±7·9 per cent (±s.d.) and 81·5±2.7 per cent respectively; whereas alginate at 57·7±7·6 per cent and the control at 48·6±10·3 per cent showed less adhesion ($P<0·001$).

To assess platelet adheson, labelled platelets were inoculated on to Dacron grafts. Mean platelet adhesion to gelatin coated Dacron was reduced by 10 per cent compared with untreated controls ($P<0·005$). In a separate experiment, a further mean fall of 13·3 per cent was achieved when the gelatin grafts were examined 24 h after inoculation with endothelial cells ($P<0·001$).

CIG and 1 per cent gelatin permit optimal endothelial cell bonding without promoting excess platelet adhesion. The addition of both substrate and endothelial cells renders the Dacron surface considerably less attractive to platelets.

1. Sharefkin JB, Latker C, Smith M, Cruess D, Claggett P, Rich NM. Early normalisation of platelet survival by endothelial seeding of Dacron arterial prostheses in dogs. *Surgery* 1982; **92**: 385–93.

Mucosal glucosamine synthetase in Crohn's disease: a protective mechanism?

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Glucosamine synthetase (GS) is a rate limiting enzyme in mucosal glycoprotein synthesis. Increased rectal GS activity has been reported in patients with ileal Crohn's disease (ICD) which may represent a protective response to toxic luminal factors[1]. To test this hypothesis, rectal GS activity was measured in patients with ICD, Crohn's proctitis (CP) and a control group before and 2, 6 and 12 weeks after defunction by an ileostomy. The effect of restoration of intestinal continuity was also assessed in Crohn's disease (CD) and controls. GS activity (mM g^{-1} h^{-1}) was assessed by the Winterburn and Phelps method[2] using the Morgan–Elson reaction.

Table *GS activity (mM g^{-1} h^{-1})*

	Prediversion	Post-diversion		
		2 weeks	6 weeks	12 weeks
Control	22·9±3·4 ($n=11$)*	18·3±2·3 ($n=11$)	18·2±3·7 ($n=9$)	24·4±5·5 ($n=35$)
ICD	34·8±4·5 (n=11)	27·9±4·6 (n=11)	19·2±3·4 ($n=10$)**	16·4±4·6 (n=5)**
CP	28·6±3·0 ($n=11$)	20·0±4·5 ($n=10$)	16·2±2·5 ($n=10$)**	31·5±7·3 ($n=6$)
	Precontinuity	**Post-continuity**		
Control	14·3±3·3 ($n=7$)	24·0±4·8 ($n=7$)	22·4±5·1 ($n=6$)	28·8±5·6 ($n=2$)
CD	14·7±2·5 ($n=9$)	25·5±3·7 ($n=9$)**	21·0±3·9 ($n=7$)	22·8±6·2 ($n=7$)

Values are means±s.e.m. *$P<0·05$, **$P<0·01$ when compared with pre-operative levels

The reduction in GS activity after diversion and increase after restoration of continuity compared with a control group suggests that a luminal factor significantly stimulates glycoprotein synthesis in Crohn's disease. This finding supports the role of a toxic component of the faecal stream in the pathogenesis of Crohn's disease.

1. Goodman MJ, Skinner JM, Truelove SC. Abnormalities in the apparently normal bowel mucosa in Crohn's disease. *Lancet* 1976; i: 275–8.
2. Winterburn PJ, Phelps CF. Purification and some kinetic properties of rat liver glucosamine synthetase. *Biochem J* 1971; **121**: 701–9.

Tissue hypoxia and leakage from intestinal anastomoses

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The relative importance of tissue hypoxia as a cause of intestinal anastomotic leakage in patients has never been established. This study assesses tissue oxygen tension (P_{t,O_2} levels in the intestine of 60 patients undergoing resection and anastomosis and relates this to subsequent anastomotic healing.

A modified Clark oxygen electrode with a linear response to oxygen ($r=0·995$, $P<0·001$) was used to measure P_{t,O_2} peroperatively from the serosal surface of the intestine. Measurements were taken before resection (baseline) and after construction (perianastomotic) of the anastomoses from the proximal and distal resection margins and from control sites. Arterial P_{O_2} was also recorded. Postoperatively, anastomotic integrity was assessed clinically and radiologically.

Anastomotic leakage occurred in five patients (all anterior resections). The mean perianastomotic P_{t,O_2} in anastomoses which leaked was lower than in intact anastomoses (t test, $P<0·01$). All four anastomoses constructed in tissue with P_{t,O_2} of <20 mmHg leaked

(Fisher's exact test, $P<0·005$). In anterior resections, lower P_{t,O_2} levels were frequently found on the proximal side of the anastomoses (paired *t* test, $P<0·01$), suggesting inadequate perfusion through the marginal artery in many cases.

In conclusion, tissue hypoxia, detectable peroperatively by this technique, appears to be an important contributory factor to anastomotic leakage in patients.

Colonic cellular proliferation rates in normal subjects: the effect of the faecal stream

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The role of the faecal stream in maintaining colonic mucosal cellular kinetics was assessed by measuring the cell birth rate (crypt cell production rate, CCPR) of normal rectal mucosa in patients undergoing faecal diversion by ileostomy for incontinence ($n=6$) or protection of an anastomosis ($n=4$). Rectal biopsies were obtained before diversion and 2, 6, and 12 weeks afterwards. The effect of restoration of intestinal continuity was assessed, at the same time points, in patients undergoing closure of ileostomy (postincontinence procedure $n=4$, post-anastomotic protection $n=5$).

CCPR was assessed by an *in vitro* stathmokinetic method[1] with vincristine induced metaphase arrest.

Table *Rectal crypt cell production rate*

Prediversion	Post-diversion		
	2 weeks	6 weeks	12 weeks
3·4±1·0 ($n=10$)	1·2±0·4 ($n=9$)*	1·7±0·4 ($n=8$)	3·3±1·5 ($n=5$)
Preclosure of ileostomy	Post-closure of ileostomy		
1·9±0·3 ($n=9$)	2·2±0·5 ($n=7$)	2·3±0·6 ($n=4$)	4·3±1·4 ($n=3$)

Values are means ± s.e.m. cell crypt^{-1} h^{-1}. *$P<0·05$ when compared with prediversion

Faecal diversion causes a significant transient reduction in rectal CCPR. These data suggest that the faecal stream has a tropic effect on mucosal cellular proliferation. The mechanism of this phenomenon is unclear.

1. Wright NA, Appleton DR. The metaphase arrest method: a critical review. *Cell Tissue Kinet* 1980; 13: 643–63.

Sustained epithelial proliferation after faecal diversion for Crohn's disease: objective evidence of mucosal recovery

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Faecal diversion for Crohn's colitis frequently produces clinical remission but there is no objective evidence of mucosal recovery. The effect of faecal diversion may be mediated by changes in mucosal cellular kinetics.

To test this hypothesis, the cell birth rate (crypt cell production rate, CCPR) of rectal mucosa in patients with ileal Crohn's disease (ICD), Crohn's proctitis (CP), and a control group was measured before and 2, 6 and 12 weeks after defunction by an ileostomy. CCPR was assessed by an *in vitro* stathmokinetic method[1]; metaphase arrest was induced in rectal biopsies with vincristine.

Table *Rectal crypt cell production rate*

	Prediversion	Post-diversion		
		2 weeks	6 weeks	12 weeks
Controls	3·4±1·0 ($n=10$)	1·2±0·4* ($n=9$)	1·7±0·4 ($n=8$)	3·3±1·5 ($n=5$)
ICD	2·8±0·6 ($n=11$)	2·0±0·7 ($n=8$)	2·1±0·8 ($n=10$)	2·1±0·5 ($n=6$)
CP	2·4±0·9 ($n=9$)	3·0±0·8 ($n=9$)	3·8±1·0 ($n=7$)	2·1±1·6 ($n=3$)

Values are means ± s.e.m. cell crypt^{-1} h^{-1}. *$P<0·05$ when compared with prediversion

In Crohn's disease the CCPR in macroscopically normal and inflamed tissue is similar to controls. The sustained proliferation rate after diversion in Crohn's disease, compared with the significant fall in the control group, may represent a regenerative mechanism promoting epithelial repair and clinical remission. This response suggests that a toxic faecal factor perpetuates the inflammatory process in Crohn's disease.

1. Wright NA, Appleton DR. The metaphase arrest method: a critical review. *Cell Tissue Kinet* 1980; 13: 643–63.

Abnormal crypt kinetics: a means of identifying subjects at risk of colon cancer

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There is considerable evidence for the role of an adenoma–carcinoma sequence in the evolution of colonic cancer. Using autoradiography, after 1 h labelling with tritiated thymidine (^{3}HTdR) of colonoscopic biopsy specimens, crypt kinetics were determined in mucosa adjacent to adenomas and in remote mucosa, and compared with kinetic measurements in mucosa from normal subjects.

In 14 patients with colonic adenomas, a significant increase in the labelling index (percentage of cells incorporating ^{3}HTdR) was found in mucosa adjacent to adenomas (16·2 per cent) and in remote mucosa (14·8 per cent) when compared with the labelling index of mucosa from 12 normal subjects (12·5 per cent; $t=18·86$, $P<0·001$ and $t=13·64$, $P<0·001$ respectively).

The position of the proliferative compartment within crypts was determined by generating cumulative labelled cell distribution curves, using the Kolmogorov–Smirnov test for statistical analysis. Irrespective of site, a significant extension of the proliferative compartment into the upper regions of crypts was found in mucosa adjacent to adenomas ($D_2=6·44$, $D_2=7·96$; $P<0·001$) and also in remote mucosa ($D_2=4·53$, $D_2=6·32$; $P<0·001$). For individual biopsies, the assessment of cumulative labelled cell distribution abnormality had a sensitivity of 17 out of 24 (71 per cent), a specificity of 24 out of 29 (83 per cent) and a positive predictive value of 17 out of 22 (77 per cent) for the detection of patients with adenomas.

This method has obvious potential in the detection of individuals at increased risk of colonic carcinoma.

A study of the effect of 4 days pre-operative lactulose on post-haemorrhoidectomy pain

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The effect of 4 days pre-operative lactulose on post-haemorrhoidectomy pain has been studied in a prospective double-blind randomized trial. All patients received lactulose on admission to hospital, 20 received lactulose for 4 days before admission, 22 received placebo.

The pre-operative lactulose group opened their bowels earlier (median time to defaecation 2·0 *versus* 3·0 days, $P=0·01$), more frequently in the first week (median number of bowel actions 9·0 *versus* 5·0, $P=0·05$) and had a shorter hospital stay than the placebo group (median 5·0 days, range 3·0–8·0 *versus* 5·0, 4·0–14·0; $P=0·03$). The pre-operative lactulose group suffered significantly less pain on defaecation for the first 4 days that they opened opened their bowels (visual analogue scores in cm: day 1, 4·4 *versus* 5·9, $P=0·05$; day 2, 4·1 *versus* 6·3, $P=0·025$; day 3, 4·5 *versus* 6·1, $P=0·05$; day 4, 4·6 *versus* 6·5, $P=0·02$), suffered significantly less pain during the first two 24-hour periods after defaecation (visual analogue scores in cm: day 1, 5·0 *versus* 7·0, $P=0·005$; day 2, 3·9 *versus* 6·1, $P=0·005$), and required significantly less analgesia per day after defaecation (0·76 g/day of paracetamol *versus* 1·29 g/day, $P=0·01$). These results show that 4 days pre-operative lactulose produces many benefits for the haemorrhoidectomy patient, including a reduction in postoperative pain.

Anal cancer and the human papillomavirus type 16

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Clinical and epidemiological evidence suggests that anal cancer and anal sexual activity are related[1,2]. The sexual transmission of human papillomavirus (HPV) type 16 is strongly associated with cervical squamous cell carcinoma[3]; anal squamous cell carcinoma may be similarly associated. We have used a specific radiolabelled HPV 16 DNA probe to examine DNA from 11 anal malignancies and 8 control haemorrhoidectomy specimens. DNA samples were digested with restriction enzymes; the resultant fragments were bound to nylon membranes by Southern transfer[4], hybridized with the probe under stringent conditions, and the membranes exposed to X-ray film. Six of eight anal squamous cell carcinomas contained HPV 16 DNA predominantly integrated into the host cell DNA. All eight control specimens were negative ($P=0\cdot007$, two-tailed Fisher's exact test). Two anal malignant melanomas and an anal adenocarcinoma were also negative. No sexual history was available for these patients, who were treated at several centres. In view of the association between anal squamous cell cancer and HPV 16 demonstrated in this investigation, a case control study is now required to investigate the prevalence of anal sexual practices in cases of anal cancer.

1. Cooper HS, Patchevsky AS, Marks G. Cloacogenic carcinoma of the anorectum in homosexual men. *Dis Colon Rectum* 1979; **27**: 557–8.
2. Austin DF. Etiologic clues from descriptive epidemiology; squamous cancer of the anus. *Natl Cancer Inst Mongr* 1982; **62**: 89–90.
3. Singer A, Campion MJ, McCance DJ. Human papillomavirus. *Br J Hosp Med* 1985: 104–8.
4. Southern E. Detection of specific sequences among DNA fragments separated by gel electrophoresis. *J Mol Biol* 1975; **98**: 503.

Tumour cyclic-AMP-binding protein (cAMP-B) in colorectal carcinoma

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Growth of colorectal cancer cell lines is inhibited by micromolar concentrations of cyclic AMP (cAMP) analogues[1]; growth inhibition may depend on the presence of type I cAMP-B protein kinase in tumour cells. To determine the feasibility of using site-selective cAMP analogues as chemotherapeutic agents in man, we have looked for the presence of appropriate cAMP-B protein kinase in colorectal cancer. Fresh tumour tissue from 28 colorectal carcinomas (Dukes': A1, B14, C13) and benign colorectal mucosa from 8 patients were analysed for cAMP-B levels using an established radioligand assay[2]. Levels of cAMP-B were higher in malignant compared with benign lesions (see *Table*). Rectal carcinomas ($n=11$) had significantly higher cAMP-B levels than colonic carcinoma ($n=17$, $P=0\cdot02$). Neither the Dukes' stage nor degree of tumour differentiation affected cAMP-B levels. Polyacrylamide gel electrophoresis demonstrated an increase of binding proteins in tumour cytosols, mainly of the type I regulatory subunit.

	Benign ($n=8$)	Colon cancer ($n=17$)	Rectal cancer ($n=11$)
cAMP-B levels	1682±337	2368±741	3796±1674

Values are means±s.d. (μM). Colon cancer *versus* control, $P=0\cdot005$; rectal cancer *versus* control, $P=0\cdot002$ (two sample t test with separate variant estimate)

Since cAMP-B is present in the cytosol of colorectal carcinoma, site-selective cAMP analogues have a potential role as chemotherapeutic agents in colorectal cancer.

1. Tagliaferri P, Katsaros D, Clair T *et al.* Growth arrest and morphological change of colon human carcinoma cell lines by selective cAMP analogues at micromolar concentrations. *Cancer Res* 1987; (In Press).
2. Miller WR, Senbanjo RO, Watson DMA. Cyclic AMP binding proteins in human breast cancer. *Br J Cancer* 1985; **52**: 531–5.

Combined sensory and motor deficit in primary neuropathic faecal incontinence

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Patients with idiopathic faecal incontinence (IFI) often report that they have no sensation of impending or actual incontinence. We have studied 11 patients with IFI (8 women) mean age (±s.d.) 56·2±16·9 years, and 9 normal controls (4 women) 56·6±15·9 years, with the technique of mucosal electrosensitivity and rectal distension for the quantitative assessment of anorectal sensation. Pelvic floor motor function was assessed by calculating fibre density (an index of denervation:re-innervation) from single fibre EMG of the external anal sphincter, pudendal nerve terminal motor latency (PNTML), and anal canal manometry.

Table *Summary of results*

	IFI		Normal controls		Mann–Whitney U test
Mucosal electrosensitivity (mA)					
upper third	18·4	(5·2–25)	5·3	(3 9–6·9)	$P<0\cdot002$
middle third	10·1	(5·7–21 4)	3·7	(1·7–7·2)	$P<0\cdot002$
lower third	8·9	(3·1–21·6)	4·4	(3 1–6·0)	$P<0\cdot02$
Fibre density	1·73	(1·21–2 18)	1·38	(1 06–1·69)	$P<0\cdot05$
Right pudendal nerve latency (ms)	2·4	(2·0–3·0)	2·0	(1 7–2·5)	$P<0\cdot002$
Left pudendal nerve latency (ms)	2·25	(1·8–3·9)	2·0	(1·8–2·15)	$P<0\cdot05$
Resting pressure (cmH$_2$O)	40	(40–120)	100	(40–120)	$P<0\cdot05$
Squeeze pressure (cmH$_2$O)	60	(0–120)	150	(100–210)	$P<0\cdot002$

Mucosal electrosensitivity showed a significant sensory deficit throughout the anal canal in IFI compared with controls. Fibre density and PNTML were significantly increased in IFI, indicating a motor-neuropathy, with concomitant decrease in anal canal manometry, compared with controls. Rectal sensation was similar in both groups. This is the first report of a significant sensory deficit in the anal canal in combination with a motor-neuropathy in a group of patients with primary neuropathic faecal incontinence.

Evidence that faecal bile acids may be involved in aetiology of bowel cancer from a prospective study of patients with ulcerative colitis

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A prospective study was undertaken between 1974 and 1985 of 102 patients with extensive ulcerative colitis, of more than 10 years duration, to test the hypothesis that higher concentrations of bile acids in faeces are associated with higher risk of developing colorectal cancer. Faeces were collected from the patients for measurement of faecal bile acid levels (FBA) the patients were regularly followed up in out-patients with rectal biopsy and colonoscopy, and the clinical outcome was carefully documented. The average faecal bile acid level among the 14 patients who developed carcinoma or definite dysplasia was significantly higher than in the 88 patients not developing dysplasia or carcinoma ($P=0\cdot001$). These results support the theory that bile acids may be involved in the pathogenesis of colorectal cancer.

Group of patients	No.	FBA concentration (mean±s.e.m.)	Length of history (years)	Men	Women	Average age in 1974 (years)
Operation						
1 Carcinoma or dysplasia	14	9·86±0·809	19	8	6	53
2 No carcinoma or dysplasia	8	7·52±0 694	14	7	1	51
3 No operation	80	7·51±0·261	16	41	39	58
Groups 2+3	88	7·51±0 242				

Hypothesis: group 1=group 2+3 ($t=3\cdot42348$, d.f.=100, $P=0\ 001$; Mann–Whitney U test=335·5, $P=0\cdot0063$)

Comparison of straight and reservoir colo-anal anastomoses following rectal excision for benign and malignant conditions

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The functional results after straight colo-anal anastomoses (SC) performed endo-anally are often variable. Lazorthes devised the colonic

'J' reservoir and anastomosed this to the anal canal transphincterically. We have employed the endo-anal route for colonic reservoir–anal anastomosis (CR + C) and have compared, in both physiological and clinical terms, our first 13 CR + C patients with 15 consecutive patients who had undergone SC anastomosis.

The two groups were well matched for mean age, male:female ratio, size and site of tumour, proximal and distal resection margins. There was no significant difference in the incidence of postoperative complications between the two groups.

	Follow-up (months)	Stool frequency/ 24 h (range)	Resting pressure (cmH_2O)	Squeeze pressure (cmH_2O)	RSV (cmH_2O)	MTV (cmH_2O)
CR + C	7 ± 4	1·4 (0·5–2)	68 ± 14	111 ± 33	83 ± 30	317 ± 121
SC	47 ± 23	2·3 (1–6·5)	71 ± 24	98 ± 38	52 ± 22	174 ± 83
			n.s.	n.s.	$P<0{\cdot}05$	$P<0{\cdot}01$

RSV, rectal sensitivity threshold volume; MTV, maximum tolerable volume

All CR + C patients had a stool frequency/24 h ⩽2 and had a formed stool, while 40 per cent of SC patients had a stool frequency/24 h > 2, and four had a loose stool. Three patients in the CR + C group and six patients in the SC group had minor incontinence; all other patients were fully continent. Compliance of the 'neorectum' was significantly increased in the CR + C group compared with the SC group.

We would suggest that a colonic reservoir should be considered whenever a colo-anal anastomosis is contemplated.

Intraluminal pressure adjacent to left colonic anastomoses

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The role of intraluminal pressure in relation to a newly fashioned colonic anastomosis has not previously been studied in humans. We have measured intracolonic pressures using four fine bore perfused tubes, and stored data in analogue and digital form. Validation included recording intraluminal pressures using four tubes at the same site in twelve patients. A total of 96 per cent of 280 pressure peaks were within 8 mmHg of each other over a range of 10–100 mmHg.

Seventy-four hours of data have been acquired over a median of nine postoperative days (range 4–17), in eight patients with the tubes sutured in position 2·5 cm either side of a left colonic anastomosis.

Before recovery of activity the intraluminal pressure remained within 10 mmHg of atmospheric pressure.

When the ileus resolved, pressure proximal to the anastomosis in excess of 10 mmHg occurred < 1 per cent of the time. Distal pressures were elevated with respect to the proximal site ($t = 12{\cdot}34$, $P < 0{\cdot}001$). Raised distal pressures occurred as either intermittent colonic waves, mean duration 20 s, mean pressure 19 mmHg (peak 80 mmHg) or as a tonic contraction for periods of 15–20 min, mean 14 mmHg (peak 45 mmHg).

The fluctuating pressure difference across an anastomosis may cause shearing stress and promote anastomotic leakage.

The aetiology of continued 'defaecation' in the presence of a loop ileostomy

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A loop ileostomy is the defunctioning procedure of choice[1] but may not guarantee complete defunction[2]. To evaluate this criticism the defunctioning efficiency of the loop ileostomy was assessed in 23 patients. Six patients experienced episodes of defaecation but only three had signs of stomal retraction.

The defunctioning efficiency was assessed by a modified radioisotope and dye technique[3]. Efficiency was assessed in the supine position to maximize overflow ($n = 7$) or during unrestricted activity ($n = 16$).

The median defunctioning efficiency (MDE) in the absence of defaecation was 99·99 per cent (range, 99·95–100·0) irrespective of body position. In three patients with defaecation but no stomal retraction the MDE was 99·97 per cent (range, 99·97–100·0). Defaecation continued despite split ileostomy formation and all three underwent proctocolectomy for acute distal disease. In three patients with defaecation and stomal retraction, the MDE was 84·7 per cent (range, 31·16–99·0). After stoma revision the MDE improved to 99·99 per cent ($P < 0{\cdot}01$).

In the absence of stomal retraction, the loop ileostomy achieves almost complete defunction, regardless of whether the proximal limb is dependent, and continued defaecation is secondary to acute distal disease. Defaecation is only due to distal overflow if there is associated stomal retraction and this is cured by stoma revision.

1. Williams NS, Nasmyth DG, Jones D, Smith AM. Defunctioning stomas: a prospective controlled trial comparing loop ileostomy with loop transverse colostomy. *Br J Surg* 1986; 73: 566–70.
2. Harper DH, Truelove SC, Lee ECG, Kettlewell MGW, Ferrall DP. Slip ileostomy and ileocolectomy for Crohn's disease of the colon and ulcerative colitis: a 20-year study. *Gut* 1983; **24**: 106–113.
3. Schofield PF, Cade D, Lambert M. Dependent proximal loop colostomy: does it defunction the distal colon? *Br J Surg* 1980; **67**: 201–2.

Pelvic floor neuropathy: a comparative study in diabetes mellitus and idiopathic faecal incontinence

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Diabetic neuropathy is common, though pelvic floor function has not been investigated in this condition. We studied 21 diabetics (DM) mean age (±s.d.) 55·3 ± 8·8 years, 18 patients with idiopathic faecal incontinence (IFI) 54·1 ± 16·8 years, and 11 age-matched controls. All diabetics had neurophysiological evidence of peripheral sensory neuropathy. None had faecal incontinence. Pelvic floor motor function was assessed by calculating fibre density (FD) from single fibre EMG of external anal sphincter; pudendal nerve terminal motor latency (PNTML); and anal canal manometry. Sensation was assessed by balloon distension of the rectum and mucosal electrosensitivity (MES) of the anal canal.

	Controls	DM	IFI
Fibre density	1·38 (1·06–1·60)	*1·82 (1·42–2·57)	*2·07 (1·21–2·37)
Mean PNTML (ms)	1·95 (1·7–2·25)	‡2·10 (1·60–2·45)	*2·50 (1·80–3·15)
MES (mA)			
Upper third	5·3 (3·4–6·9)	†*8·2 (3·1–13·5)	*11·2 (5·2–25)
Middle third	3·7 (1·7–7·2)	*6·2 (2·7–13·5)	*7·0 (2·1–21·4)
Lower third	4·0 (2·0–6·2)	*6·2 (2·9–17·5)	*5·7 (8·2–21·4)
Resting pressure (cmH_2O)	90 (40–120)	‡80 (24–120)	*40 (20–120)
Squeeze pressure (cmH_2O)	140 (50–210)	†142 (40–320)	*40 (0–160)

Results shown are median values with ranges in parentheses. Mann–Whitney *U* test: $^*P < 0{\cdot}01$, compared to controls; $^\dagger P < 0{\cdot}01$ and $^\ddagger P < 0{\cdot}05$, compared to IFI

FD was significantly increased in DM and IFI compared with controls. MES showed a significant sensory deficit through the anal canal in DM and IFI. PNTML and manometry were similar to controls in DM, but in IFI were significantly increased and decreased, respectively. Rectal sensation was similar in all groups. This proximal asymptomatic sensorimotor pelvic floor neuropathy is a new finding in DM and is in contrast to the symptomatic neuropathy of IFI.

Cholecystokinin provocation does not predict outcome in acalculous biliary pain

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Interest continues in cholecystokinin provocation to identify patients with acalculous biliary pain who will benefit from surgery. One recent study suggests that if symptoms are reproduced by cholecystokinin infusion, cholecystectomy always results in improvement[1].

We have performed cholecystokinin provocation tests in 63 patients thought to have acalculous biliary disease (58 females, 5 males); mean age 41 years). After an overnight fast, two infusions, namely cholecystokinin (0·05 units kg^{-1} min^{-1}) or saline control, were administered in a double blind randomized manner over 20 min. Ten patients (nine women, one man) had their symptoms reproduced by cholecystokinin and the test was considered positive. One patient had pain with both infusions and the remaining 52 experienced no effects or reported 'wind' discomfort only. These were considered negative tests.

Cholecystectomy was performed in 26 patients because of continued symptoms. Three patients had alternative causes for their pain at laparotomy. Of the 23 evaluable patients, 19 are improved at mean follow-up of 6 months (range 1–15 months). A total of 4 of the 5 positive patients are improved and 15 of the 18 negative patients are improved (83 per cent). We conclude that the cholecystokinin provocation test does not identify patients who will improve after cholecystectomy.

1. Lennard TWJ, Farndon JR, Taylor RMR. Acalculous biliary pain: diagnosis and selection for cholecystectomy using the cholecystokinin test for pain reproduction. *Br J Surg* 1984; **71**: 368–70.

A prospective randomized clinical trial comparing total and partial fundoplication in the surgical treatment of gastro-oesophageal reflux

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Total and partial fundoplication has been advocated for the surgical treatment of gastro-oesophageal reflux (GOR). Both procedures will control reflux symptoms in over 85 per cent of patients, but it has been reported that the Nissen operation may be associated with late postoperative dysphagia and the 'gas bloat syndrome' in 13 per cent of patients[1]. The aim of this study was to compare, prospectively, the Nissen total fundoplication (360° wrap) with the Lind partial fundoplication (300° wrap)[2] in the treatment of patients with GOR.

Fifty-two patients were randomized to undergo a Nissen or Lind antireflux procedure. Each group was comparable in number, mean age (47 years) and sex distribution (eight women). Initial assessment was clinical using a modified Visick score, by endoscopy, standard manometry and 22-h intra-oesophageal pH monitoring. Early postoperative clinical assessment was by endoscopy, manometry, pH recording, and clinical assessment performed 'blind' by an independent observer at between 6 and 28 months after operation. Statistical analysis was by χ^2 test for pre- and postoperative symptom score, and by the paired t test for the results of manometry and pH studies.

Both groups of patients had significant improvement in the results of intra-oesophageal pH monitoring and for the prevalence of heartburn and regurgitation ($P < 0.001$) after operation. The incidence of early and late dysphagia was similar (Nissen, five and one; Lind, five and zero, respectively). Troublesome 'gas bloat' at early and late assessment was more frequent after the Nissen operation (five and three) than the Lind (five and one) but this failed to reach significance.

These results suggest that both the Nissen total fundoplication and Lind partial fundoplication are equally successful in the surgical treatment of GOR.

1. Bushkin FC, Neustein CL, Parker TH *et al.* Nissen fundoplication for reflux peptic oesophagitis. *Ann Surg* 1977; **185**: 672–7.
2. Lind JF, Burns CM, MacDougall JTA. Physiological repair for hiatus hernia: a manometric study. *Arch Surg* 1965; **91**: 233–7.

Post-trial surveillance of mortality in bleeding peptic ulcer disease

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Early surgery in patients over the age of 60 with bleeding peptic ulcers was shown to have a lower mortality than delayed operation (4 *versus* 15 per cent)[1]. As these results were criticized on statistical grounds, we have audited our results but have deliberately excluded endoscopic criteria as an indication for operation. Our criteria in patients over 60 years are: 4 units blood for volume replacement, one rebleed or >8 units blood/24 h, and for younger patients 8 units blood for volume replacement, two rebleeds or >12 units blood/24 h.

There were 254 consecutive admissions with bleeding peptic ulcers over 3 years: 155 (61 per cent) were over age 60. Forty-nine patients (19 per cent) underwent emergency surgery with three postoperative deaths (6 per cent). Overall mortality was 4 per cent (ten deaths). Patients under 60 years had an operation rate of 16 per cent and one death, compared with 21 per cent (n.s.) and nine deaths (5.8 per cent $P < 0.05$) in patients aged over 60. By eliminating endoscopic stigmata alone as an indication for surgery, we have reduced our operation rate in patients over 60 years from 59 to 21 per cent ($P < 0.005$) with no effect on mortality. We have sustained a mortality of only 4 per cent for bleeding peptic ulcer disease, and believe that the conclusions of our trial are correct since early surgery is effective and safe.

1. Morris DL, Brearley S, Hawker PC *et al.* Optimal timing of operation for bleeding peptic ulcer: prospective randomised trial. *Br Med J* 1984; **288**: 1277–80.

Intragastric fibrinolysis in bleeding peptic ulcer disease

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Bleeding peptic ulcer disease remains a common problem with a mortality rate of over 10 per cent in many series. Little is known, however, about aetiology of bleeding or rebleeding in these patients. We have studied the role of the excessive fibrinolytic activity in gastric juice, due to duodenogastric trypsin reflux.

Gastric juice was taken from 32 patients presenting with upper GI haemorrhage (DU, 11; GU, 9) and 31 control patients (DU, 10, GU, 8). Fibrinolytic activity of aspirated gastric juice was assessed using fibrin plates[1], and trypsin assayed using a colorimetric method[2].

Fibrinolytic activity was found to be present in 20 patients (63 per cent) with upper GI bleeding, and only 4 (13 per cent) of controls ($P < 0.005$). Trypsin was detected in all gastric juice samples showing fibrinolysis. Fibrinolytic activity was present in 22 out of 29 samples with pH > 4, and only 2 out of 34 at lower pH ($P < 0.005$). Fibrinolytic activity was seen in six of eleven patients with bleeding DU (55 per cent), but only one of ten control DU patients (10 per cent) ($P < 0.025$). There was no significant difference in fibrinolytic activity with bleeding or non-bleeding gastric ulcers.

We conclude that patients with upper GI haemorrhage show increased fibrinolytic activity in gastric juice, compared with non-bleeding controls.

1. Astrup T, Mullertz S. The fibrin plate method for detecting fibrinolytic activity. *Arch Biochem Phys* 1952; **40**: 236–351.
2. Blackwood C, Mandl I. An improved test for the quantitative determination of trypsin, trypsin like enzymes and enzyme inhibitors. *Analytical Biochemistry* 1961; **2**: 370–9.

A comparison of the value of oesophageal manometry and pH studies in selecting patients for antireflux surgery

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Some authorities recommend that before antireflux surgery patients should undergo a pH study to establish the diagnosis firmly, and manometry to exclude a motility disorder. Between January 1979 and July 1984, we performed endoscopy, 24 h pH monitoring and manometry in all 401 patients referred for evaluation of oesophageal symptoms.

Manometric diagnosis	Number of patients	Oesophagitis	+ve pH study	Nissen fundoplication (Visick 1 and 2)
Normal	146	10 (7)	39 (27)	(26, 85)
Non-specific motility disorder	205	23 (11)	99 (48)	(56, 79)
Diffuse oesophageal spasm	20	—	2 (10)	—
'Nutcracker' oesophagus	17	—	5 (29)	(2, 2)
Achalasia	8	—	—	—
Hypertensive sphincter	4	—	—	—
Scleroderma	1	—	—	—
Total	401	33 (8)	145 (36)	(84, 82)

Values in parentheses are percentages. Results for Nissen fundoplication are percentages of patients in Visick grades 1 and 2

The majority of the patients either had normal manometry or a non-specific motility disorder (NSMD), and in one-third of these there was significant gastro-oesophageal reflux on pH studies. Eighty-four patients (21 per cent) underwent a Nissen fundoplication because of failure of medical treatment and a positive pH study, but only 39 per cent had oesophagitis; 82 per cent had a good result (Visick 1 and 2) two or more years after surgery, despite the presence of a NSMD in the majority of cases.

Pre-operative pH monitoring of the oesophagus is useful in establishing the diagnosis of gastro-oesophageal reflux when there is no oesophagitis on endoscopy. Manometry, however, is of little value as an NSMD is commonly associated with reflux and does not lead to a poor result after antireflux surgery.

Endoscopic mapping of human gastric blood flow

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Post-mortem injection studies have demonstrated that the ulcer-prone areas of the stomach and duodenum have fewer mucosal arterioles[1], but physiological evidence of poorer perfusion is lacking.

We have studied 19 patients, median age 70 (range 27–83) using the non-invasive, Laser Doppler (LD) technique. Flux measurements were made during gastroscopy under diazepam sedation, using the Periflux Pf2 instrument. Readings were made at nine sites: distal oesophagus, proximal, mid and distal stomach on greater and lesser curves, and pre- and postpylorus.

In all cases, the stomach was macroscopically normal. Flux varied from 40±28 V (mean±s.d. arbitrary units of flow) in the antrum to a maximum of 92±35 V on the lesser curve. In the proximal stomach the mean value at each site exceeded 70 V, whereas none of the five distal gastric sites had a mean value above 56 V. Overall flux in the proximal stomach, at 77·5±39·8 V, was significantly greater than that of 48·5±31·2 V in the antrum and pylorus ($P<0{\cdot}001$, Student's *t* test).

This *in vivo* study demonstrates marked regionality of blood flow in the normal stomach and duodenum, being least in the ulcer-prone areas.

1. Piasecki C. Role of ischaemia in the initiation of peptic ulcer. *Ann R Coll Surg Engl* 1977; **59**: 476–8.

The value of endoscopic surveillance in the early detection of malignant change in Barrett's oesophagus

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Estimates of the risk of adenocarcinoma developing in Barrett's columnar lined oesophagus vary greatly and most of the data previously presented has been based on prevalence. We present a prospective study of 56 patients with columnar lined oesophagus diagnosed in the 10-year period between 1977 and 1986, and followed up with regular endoscopy and biopsy. Of the 56 patients, 31 were men; their mean age was 62 years (range 22–84) and the mean follow-up was 3 years. During follow-up the squamocolumnar mucosal junction was observed to progress up the oesophagus in 11 patients, but such progression did not increase the risk of malignancy ($\chi^2=0{\cdot}94$, n.s.). During the study, seven patients developed severe dysplasia in the columnar epithelium, two progressed to carcinoma *in situ*, and in three patients an invasive adenocarcinoma developed, two of whom had previously been noted to have dysplasia and carcinoma *in situ*. Diagnosis depended largely upon biopsy evidence because in only one of the three patients was there clear macroscopic evidence of malignancy. These figures indicate that carcinoma occurred once in every 56 patient-years follow-up, and the relative risk was 67 times greater than that of the general population of this age and sex distribution.

These findings provide clear evidence that endoscopic surveillance is important in the early detection of malignant change complicating Barrett's oesophagus.

The possible role of asbestos in gastric carcinogenesis

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There is some epidemiological evidence to suggest that workers exposed to asbestos have an excessive mortality from gastric cancer[1], and it has been postulated that the high incidence of gastric cancer in Japan may be due to contamination of their polished rice by asbestos[2].

Scanning electron microscopy was performed on specimens of stomach taken from six patients with histologically proven gastric cancer and on three patients undergoing gastric resection for benign disease. In five of the six patients with gastric cancer unknown fibres were found in the tumour tissue and, in one patient, in the premalignant mucosa surrounding them. Simultaneous X-ray micro-analysis of these fibres has shown them to contain silicon, magnesium, calcium and iron and their molar ratios strongly mimic the known X-ray elemental profile of tremolite asbestos. No fibres have been identified in any of the control tissue.

These findings suggest that mineral fibres might play an important role in the pathogenesis of gastric cancer.

1. Levine DS. Does asbestos exposure cause gastrointestinal cancer? *Dig Dis Sci* 1985; **30**: 1189–98.
2. Merliss RR. Talc and asbestos contamination of rice. *JAMA* 1971; **216**: 2144.

Enprostil therapy for alkaline reflux gastritis: an endoscopic, histological and kinetic assessment

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Enprostil, a synthetic dihydroprostaglandin E_2, is known to protect the gastric mucosa from harmful agents. The aim of this study was to investigate its effect in patients with symptomatic alkaline reflux gastritis (ARG) secondary to gastric surgery performed 3–24 years (mean 10·9 years) previously.

Ten patients received placebo followed by Enprostil (35 μg b.d.) each for a 2-month period in a single blind fashion. Gastroscopy was performed (by an independent observer) on entry and after each treatment period. The extent of mucosal erythema was recorded (0 = normal, 4 = entire gastric mucosa affected) and biopsies were taken at 1, 3 and 6 cm away from the stoma along the posterior gastric wall. Histological scoring was performed for dysplasia, metaplasia, atrophy and gastritis[1] and cell kinetic studies by ^{3}H thymidine incorporation (TLI).

	Baseline	Placebo	Enprostil	
Endoscopy score	2·16±0·1	2·32±0·1	0·4 ±0·8	$P<0{\cdot}001$
Dysplasia score				
1 cm	1·12±0·7	1·4 ±0·3	0·56±0·5	$P<0{\cdot}03$
3 cm	1·11±0·3	0·98±0·4	0·67±0·67	$P<0{\cdot}03$
6 cm	1·0 ±0	0·9 ±0·3	0·67±0·5	n.s.

The mean (±s.d.) scores are given

Enprostil markedly reduced mucosal erythema and histological evidence of dysplasia.

Atrophy, metaplasia, gastritis and TLI were unaffected. No side effects were noted.

These results are similar to those achieved by surgical procedures which divert bile away from the stomach[2]. The reduction in dysplasia, in the presence of continuing gastritis, suggests that Enprostil is exerting a specific protective effect on the gastric mucosal cells.

1. Watt P, Sloan JM, Kennedy TL. Changes in gastric mucosa after vagotomy and gastrojejunostomy for duodenal ulcer. *Br Med J* 1983; **287**: 1407–10.
2. Watt P, Sloan JM, Spencer A, Kennedy TL. Histology of the postoperative stomach before and after diversion of bile. *Br Med J* 1983; **287**: 1410–12.

Applied potential tomography in the evaluation of congenital hypertrophic pyloric stenosis

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Diagnosis of hypertrophic pyloric stenosis in infants is often difficult due to the variability of symptoms and the lack of objective investigation of gastric emptying (GE). Applied potential tomography (APT) is a new non-invasive technique which can measure GE in infants by detecting changes in tissue resistivity via surface electrodes after ingestion of a liquid test meal.

Nineteen infants (age 2–10 weeks) were imaged for up to 60 min after ingestion of 100 ml Dextrolyte (Cow and Gate, UK). Twelve infants had clinical symptoms of hypertrophic pyloric stenosis (HPS), seven of whom subsequently underwent surgery. Seven infants had no HPS symptoms and acted as controls.

The time taken to empty 50 per cent of the liquid meal was expressed as $T_{\frac{1}{2}}$. The median $T_{\frac{1}{2}}$ in the control group was 22 min (range 7–34 min) compared with $T_{\frac{1}{2}}$ 38 min (range 38–52 min) in the symptomatic operated group ($P = 0{\cdot}0001$). In the five infants who did not undergo surgery, and whose symptoms subsequently resolved, $T_{\frac{1}{2}}$ was 27 min (range 10–45 min); this was not significantly different from controls but was still faster ($P = 0{\cdot}037$) than the operated group.

We have found APT to be a useful technique in the evaluation of gastric emptying in hypertrophic pyloric stenosis when clinical diagnosis is uncertain.

Bile crystal analysis for the detection of gallstones associated with acute pancreatitis

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In patients with acute pancreatitis ultrasonography, biochemical tests and ERCP are useful in the detection of gallstones. Despite these techniques, the proportion of patients with 'idiopathic' pancreatitis is still reported as 25 per cent or more. The aim of the present study was to assess the value of gallbladder bile crystal analysis (cholesterol and/or calcium bilirubinate crystals) in these patients.

Bile was collected at duodenoscopy in patients fasted overnight after IV administration of 100 units of cholecystokinin–pancreazymin (Boots, UK). Samples were examined by direct and polarizing microscopy by an independent observer at 20°C and after 24-hour incubation at 37°C.

The technique was assessed in 30 control patients without pancreatitis (17 with gallstones, 13 without gallstones) and 25 patients with pancreatitis (11 due to gallstones, 14 due to alcohol) and was subsequently applied to 13 patients initially diagnosed with 'idiopathic' pancreatitis.

Patient group	Crystals Present	Crystals Absent	Sensitivity (%)	Specificity (%)
Control				
Gallstones ($n = 17$)	11	6	65	92
No gallstones ($n = 13$)	1	12		
Acute pancreatitis				
Gallstones ($n = 11$)	7	4	64	100
Alcoholic ($n = 14$)	0	14		

Four of the patients with 'idiopathic' pancreatitis had crystals (31 per cent). Three of these patients had gallstones confirmed at cholecystectomy, two of whom had crystals present pre-operatively.

Bile crystal analysis has a high specificity and may be usefully applied to patients with 'idiopathic' pancreatitis—its wider use is recommended.

Changes in lower oesophageal sphincter pressure after gastroplasty

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There is limited evidence to suggest that vertical banded gastroplasty (VBG) is an antireflux operation. The mechanisms for competence of the lower oesophageal sphincter are complex and not fully understood. All antireflux operations in current practice have been reported to increase the lower oesophageal sphincter tone in most patients.

As part of an extended study of the physiological consequence of VBG performed for morbid obesity, oesophageal manometry was performed on 12 patients before and after surgery. The lower oesophageal sphincter pressure was measured by a standard 'pull-through' technique. The manometric studies were repeated on all patients between 1 and 4 months postoperatively.

The mean pre-operative lower oesophageal sphincter pressure was 24·7 ± mmHg (± s.d. 9·89, range 12·5–45). This increased postoperatively to a mean of 33·3 mmHg (± s.d. 9·96, range 24–58). Using a paired t test analysis this difference was found to be statistically significant ($P < 0{\cdot}05$).

Pre-operatively, three of the twelve patients had symptoms of gastro-oesophageal reflux. All three patients became asymptomatic postoperatively and none of the patients has had any dyspeptic symptoms post-VBG.

We conclude that vertical banded gastroplasty has an antireflux effect. Modification of this procedure may have a place in the treatment of gastro-oesophageal reflux in non-obese patients.

Blowing hot and cold on peptic disorders

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Historically, an association has been alleged between hot drinks and some diseases of the upper gastrointestinal tract, but there are little reliable data on the subject. In this study the usual temperature at which hot drinks were consumed was measured in patients with peptic diseases and in asymptomatic volunteers. In 64 controls, the median temperature was 56·0°C, range 47·5–65·0°C. In 57 patients with oesophageal, gastric and duodenal disease, the median temperature was 62·0°C, range 53·0–73·0°C ($P < 0{\cdot}001$ Mann–Whitney U test).

To study temperature profiles of ingested food and drink, a system has been developed to record intraluminal temperature simultaneously at 10/s from six sites. In controls after hot food, intraluminal temperature reached peaks of 63, 49·5 and 42°C in the oesophagus, stomach and duodenum, respectively. Hot coffee produced peak temperatures of 53·5, 45 and 42°C. After cold drinks the temperature fell to 7°C in the oesophagus, 19°C in the stomach and 25°C in the duodenum. The temperature changes varied in duration (see *Table* for examples).

	Length of time above temp level after hot food (min.s)			Length of time below temp level after cold drink (min.s)		
	>37°C	≥40°C	≥44°C	<37°C	≤34°C	≤30°C
Mid-oesophagus	6.20	4.51	3.16	0.30	1.56	1.19
Body stomach	0.30	13.12	5.55	0.30	9.20	1.45
Duodenal bulb	0.30	0.0	0.0	11.39	4.34	1.45

Repeated exposure to these extremes of temperature may alter the properties of adherent mucus and the cytoprotective function of the gastrointestinal lining. If so, appropriate advice might be relevant to patients with peptic disorders.

Posterior vagotomy and stapling of the anterior gastric wall for duodenal ulcer

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We have evaluated a simple technique involving posterior truncal vagotomy followed by stapling of the anterior gastric wall (TA90) from the incisura to the fundus, to reduce acid secretion whilst preserving antral innervation.

Postoperative assessment was by endoscopy and Congo red spraying to identify innervated mucosa, gastric secretory studies, isotope solid and liquid emptying studies and clinical follow-up.

All 21 patients had endoscopically proven duodenal ulcer; no significant postoperative complication occurred. Mean operative time was 48 (±9) min and postoperative stay 5·5 (±1·5) days.

At postoperative endoscopy, one prepyloric ulcer was diagnosed. Dye spraying revealed the area between the mid lesser curve and the staple line to be acid secreting. A mean reduction of 53 per cent in basal acid output was seen together with a 47 per cent reduction in peak acid output (similar to HSV).

One patient complained of bloating after meals. Liquid emptying for the group was within the normal range ($T_{\frac{1}{2}} = 14$ min, range 4–39) as was solid emptying ($T_{\frac{1}{2}} = 120$ min, range 60–160).

This easily performed technique for selectively denervating the stomach may well be clinically useful where a technically easier and rapid procedure would be advantageous.

The bloated abdomen after antireflux surgery

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The incidence of 'gas bloat syndrome' (GBS) after antireflux surgery is unknown and treatment is unsatisfactory. In this study, the incidence of late GBS was sought and new treatment was evaluated by symptomatic assessment and objective tests. Ninety postoperative patients, mean time 4·8 years, were sent a scored symptomatic questionnaire[1]. Of the 54 respondents 40 reported troublesome bloat, with a mean symptom score, 36·78. A cohort of 20 patients with most severe symptoms (∓50·9) were investigated and treated by prokinetic stimulation.

Baseline parameters, including symptom score, gastric emptying[2], intestinal transit[3] and sequential blood glucose assay, were measured after a solid meal. Treatment by Cisapride 4 mg IV then 10 mg PO t.d.s. was given. Measurements were repeated after 1 week of therapy.

Patients improved with therapy. Symptom scores fell from ∓ (±s.e.m.) 50·9±4·67 before (B) to ∓24·8±3·9 (P<0·001) after (A) treatment. Transit times fell from ∓153±11·9 (B) to ∓84·47±8·89 (A) (P<0·001). Gastric emptying and blood glucose levels were unaffected.

In conclusion, GBS is common after antireflux surgery. Cisapride relieves symptoms of postprandial bloating by stimulating intestinal transit, rather than gastric emptying, and it does not induce hypoglycaemia.

1. Bates S, Sjoden PO. Registration of pain in a psychological perspective scan. *J Gastroenterol* 1985; **20** (Suppl. 109): 15–18.
2. Heading RC, Nimmo J, Prescott LF, Tothill P. The dependence of paracetamol absorption on the role of gastric emptying. *Br J Pharmacol* 1973; **47**: 415–21.
3. Bond JH, Levitt MD. Investigation of small bowel transit time in man utilising pulmonary hydrogen [H_2] measurements. *J Lab Clin Med* 1974; **85**: 546–7.

The influence of prophylactic infusions of pooled human IgG on endotoxin profiles following thermal injury

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Endotoxin is released into the circulation after thermal injury. As a result, suppressor cell activity is stimulated (thus predisposing to septic complications) and morbidity and mortality are increased. In order to counteract the detrimental effects[1,2] an accurate plasma profile is desirable.

Using the limulus amoebocyte lysate assay (accurate to ±5 pg/ml) we measured plasma endotoxin levels for the initial 5–10 days in 70 burned patients (range, 10–90 per cent body surface area (BSA) mean, 26·1 per cent). Ages varied from 10 to 95 years (mean, 36·3). Included were 20 patients who received pooled human IgG infusions prophylactically in a controlled double blind study.

Endotoxin levels were elevated for 5–8 days, and subsequently during septic episodes. They peaked on days 3 and 4 and correlated with percentage BSA burned. Values were not related to mechanism of injury or age but were reduced by IgG.

In conclusion, in burns the plasma endotoxin levels correlate with extent of tissue injury. Pooled human IgG which diminishes endotoxin levels as effectively as regimens previously described[1,2] has therapeutic potential.

1. Baumgartner J, Glauser M, McCutchan J. Prevention of Gram negative shock and death by antibody to endotoxin core glycolipid. *Lancet* 1985; ii: 59–63.
2. Munster A, Winchurch R, Thupari J, Ernst C. Reversal of postburn immunosuppression with low dose polymyxin. *Br J Trauma* 1986; **26**: 995–9.

Reticulo-endothelial failure in chronic intra-abdominal sepsis: the role of opsonic fibronectin

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Delayed bacterial clearance may contribute towards the complications of severe sepsis[1] but it is unclear whether this is due to deficiency of opsonin or intrinsic macrophage dysfunction. Low levels of opsonic fibronectin accompany severe sepsis but, despite restoration of opsonin levels with FN therapy, survival has not been significantly improved in patients with intra-abdominal sepsis[2]. Alteration in RES function can be detected *in vivo* using low dose technetium tin colloid[3] (TTC).

We have investigated the effect of intra-abdominal abscess on RES function and plasma fibronectin levels. The blood clearance and hepatic uptake of TTC (0·002 mg kg^{-1}) was measured in rabbits 2 weeks after either induction of sepsis (appendix abscess, $n=6$) or sham laparotomy ($n=6$). Plasma fibronectin levels were determined repeatedly during the 2-week period.

	Sham laparotomy	Intra-abdominal abscess
Blood clearance ($T_{\frac{1}{2}}$ min)	0·60±0·08	1·51±0·26*
Hepatic uptake (%IDg^{-1})	1·00±0·09	0·72±0·04*
Fibronectin (change from control, %)		
72 h	5·84±3·74	24·29±3·96*
2 weeks	11·70±2·87	12·94±5·34

The mean±s.e.m. values are given. *P<0·05, Mann–Whitney U test

There was a delay in the blood clearance, with reduced hepatic uptake of TTC in the intra-abdominal abscess group. Plasma fibronectin levels were raised at 72 hours (early sepsis), returned to normal at 1 week, and rose again in the second week (prolonged sepsis).

It is concluded that plasma fibronectin is raised in early sepsis in rabbits with impaired RES function but does not become depressed during prolonged intra-abdominal sepsis. Therefore, impaired RES function in intra-abdominal abscess may not be due to opsonin deficiency but to intrinsic Kupffer cell dysfunction.

1. Pardy BJ, Dudley HAF. Post-traumatic pulmonary insufficiency. *Surg Gynecol Obstet* 1977; **144**: 259–69.
2. Lundsgaard-Hansen P, Doran JE, Rubli E *et al.* Purified fibronectin administration to patients with severe abdominal infections. A controlled clinical trial. *Ann Surg* 1985; **202**: 745–59.
3. Chadwick SJD, Aldridge MC, Dudley HAF. Detection of reticuloendothelial blockade with low dose test agent. *Br J Exp Pathol* 1985; **66**: 483–91.

The effect of abdominal surgery upon graded exercise

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Muscle weakness is a common feature of the catabolic response to operative trauma and sepsis[1]. One effect of muscle weakness might be to increase the energy cost of performing simple tasks, for example in mobilization during the early postoperative period.

The metabolic cost of performing work was studied in six patients (4M:2F, mean age 57 years) admitted for elective abdominal surgery. Oxygen consumption ($\dot{V}_{O_2}$), active energy expenditure and metabolic cost (mets = oxygen consumption during exercise/oxygen consumption at rest) were determined by treadmill walking at a predetermined pace and gradient on the day before surgery and again on the third postoperative day. Respiratory gas exchange was monitored continually by ergospirometry and heart rate recorded by ambulatory ECG. Measurements were made during the fourth minute of exercise, at which time a steady state was assumed[2].

	Heart rate (beats min^{-1})	Peak flow (l min^{-1})	$\dot{V}_{O_2}$ (ml min^{-1} kg^{-1})	Active energy expenditure (kJ min^{-1})	Mets
Pre-op.	79±8	400±14	8·0±1·4	10·1±1·7	2·3±0·4
Postop.	104±7	209±32	10·3±0·9	13·0±1·4	2·9±0·3
P	<0·03	<0·001	<0·02	<0·02	<0·03

Values are means±s.e.m. P values are obtained from the paired Wilcoxon test

These data suggest a 30 per cent increase in the energy cost and cardiorespiratory effort required to perform simple tasks in the early postoperative period. This will have implications in terms of mobilization after abdominal surgery and may be important in the development of the postoperative fatigue syndrome.

1. Moore FD, Ball MR. *The Metabolic Response to Injury.* Springfield Illinois: C.C. Thomas 1952.
2. Masironi R, Denolin H. *Physical Activity in Disease Prevention and Treatment.* Piccin/Butterworths, 1985.

Glutamine-enriched nutrition decreases intestinal injury and increases nitrogen retention

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Damage to the intestinal mucosa occurs after starvation, ischaemia, radiotherapy and chemotherapy. Preservation may be enhanced by glutamine (Gln), a major oxidative fuel for the mucosa not provided in standard parenteral formulae. To evaluate the effects of Gln after injury, 5-fluorouracil (5FU) was administered in various doses to 49, 200 g Wistar rats receiving parenteral nutrition (TPN) with or without Gln. Four days later mucosal cellularity was measured by DNA, protein, and histological analysis.

	Dose of 5-fluorouracil (mg/kg)				Anova
	0	100	150	200	*P* value
DNA (μg/cm)					
Control	136± 6	120±14	80± 7	120± 9	
Gln	181± 6	166±19	117±13	142± 9	<0·01
Villus ht (μ)					
Control	356±11	300±10	247±11	239±16	
Gln	422±14	360±15	320±38	299±21	<0·05

The mean ± s.e.m. results are given

Severe mucosal damage was caused by 5FU but Gln decreased this intestinal injury. When TPN was given for the 5 days preceding 5FU, a significant increase in nitrogen retention (control, 736±149; Gln, 1106±85 mg nitrogen/10 days, $P<0{\cdot}05$), a trend towards increased survival (control, 6/12; Gln, 10/12), and similar intestinal changes occurred. These data suggest an important role for glutamine in minimizing mucosal damage in the intestine after injury, and possibly in attenuating the catabolic response associated with major illness.

The effect of SMS 201-995 on the growth and development of hepatic metastases

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Since reticulo-endothelial system (RES) inhibitors promote tumour growth[1], the present study was carried out to establish whether an RES stimulant, SMS 201-995 (reference 2) had any effect on the growth and development of liver metastases.

Hepatic metastases were induced in Fisher rats by intraportal injection of 4×10^7 Walker cells. An experimental group ($n=20$) received 2 μg SMS 201-995 SC b.d., commencing on the day of inoculation. Control animals ($n=20$) were dosed similarly with isotonic saline. All rats were killed 3 weeks later and the extent of liver replacement by tumour was assessed. Hepatic and splenic RES activity was determined by the uptake of ^{99m}Tc sulphur colloid, and the effects of SMS on Walker cell growth were measured both *in vitro* and *in vivo*.

SMS 201-995 significantly inhibited the growth and development of hepatic metastases ($P<0{\cdot}05$ Mann–Whitney *U* test). Thus in two animals there were no tumours, and, in a further twelve, solitary metastases (1–2 cm diameter) were present. In four rats treated with SMS 25 per cent of the liver was replaced by tumour. In contrast, in control rats the degree of liver replacement by tumour varied between 60 and 90 per cent. SMS stimulated the growth of Walker cells *in vitro* but had no effect *in vivo*. RES activity was stimulated by SMS, this effect being particularly marked in the liver (liver:blood ^{99m}Tc sulphur colloid SMS 4·41±0·45, controls 2·20±0·41, $P<0{\cdot}02$ Mann–Whitney).

These results clearly indicate that SMS 201-995 significantly inhibits the growth and development of experimentally derived hepatic metastases, possibly through RES stimulation.

1. Pearson HJ, Anderson J, Chamberlain J, Bell PRF. The influences of Kuppfer cells on the development of liver metastases following the intraportal injection of tumour cells. *Br J Surg* 1985; **72**: 402.
2. Baxter JN, Jenkins SA, Day DW, Shields R. Effect of a somatostatin analogue (SMS 201-995) on hepatic and splenic reticulo-endothelial function in the rat. *Br J Surg* 1985; **72**: 1005–8.

Wound healing in tumour bearing rats given total parenteral nutrition

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In a previous study we demonstrated an impairment of abdominal wound healing ability in anorexic weight-losing Fisher 344 rats bearing a malignant MCA sarcoma. To see if this impairment could be reversed by the provision of total parenteral nutrition (TPN) male Fisher rats ($n=8$/group; weight, 250–300 g) underwent both a midline laparotomy incision and insertion of a central venous catheter into the right jugular vein. We studied three non-tumour bearing groups: catheter but no infusion (NTB sham), saline infused (NTB Sal) and TPN infused (NTB TPN); and two tumour bearing groups: saline infused (TB Sal) and TPN infused (TB TPN). Seven days later blood was taken for measurement of haematocrit and albumin and the rats were killed. The abdominal wall was excised and tensile strength of the musculofascial and skin layers were measured separately using an Instron materials tester. The wound edges were excised for measurement of hydroxyproline.

	NTB Sham	NTB Sal	NTB TPN	TB Sal	TB TPN
Tensile strength					
Skin	763±95	1095±83	970±57	522±45*	463±58*
Muscle	655±68	846±77	938±57	350±33*	315±69*
Hydroxyproline (nmol/mg)					
Skin	67·0±7·2	76·1±6·6	79·8±11·7	34·5±3·4*	51·3±4·3*
Muscle	24·8±2·2	23·5±2·6	25·6± 3·4	11·5±2·6*	12·41±1·5*
Albumin (g/dl)	3·33±0·17	3·68±0·26	3·37±0·29	3·11±0·25	3·36±21
Haematocrit	43±3	40±3	43±4	31±5*	30±4*

* $P<0{\cdot}01$, Duncan's multiple range test

Tensile strength, hydroxyproline and haematocrit were significantly reduced in tumour bearing, compared with non-tumour bearing, rats and were not improved by administration of TPN.

In conclusion, the presence of an advanced cancer results in impaired wound healing which, although associated with poor nutritional status, may not be correctable with nutritional supplementation.

Improved utilization of hyponitrogenous–hypocaloric peripheral vein feeding with biosynthetic human growth hormone after surgery

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Previous studies have demonstrated that biosynthetic human growth hormone (BSHGH) improves nitrogen balance and increases fat oxidation in patients receiving either maintenance 5 per cent dextrose or eucaloric parenteral nutrition. This study investigates the effect of BSHGH on nitrogen balance and energy metabolism in patients receiving a hyponitrogenous (7 g N day^{-1}) and hypocaloric (500 kcal from glucose and 450 kcal from fat) regimen, administered through a peripheral vein for the first 7 days after major abdominal surgery. Six patients received BSHGH 0·1 mg kg^{-1} day^{-1} and five placebo. The BSHGH group were significantly heavier (mean 62·5, range 53–84 kg) than the placebo group (mean 50·8, range 42–58 kg). Four patients failed to complete the 7-day study, two (placebo and BSHGH) because of severe phlebitis and two (BSHGH) because of hyperglycaemia.

	Nitrogen balance (g N day^{-1})				Fat oxidation (%REE)			
Day	Placebo	(*n*)	BSHGH	(*n*)	Placebo	(*n*)	BSHGH	(*n*)
C	−5·2±0·7	5	−5·6±0·4	6	26±10	5	32±5	6
1	−1·0±1·0	5*	0·8±0·9	6	21±5	5	44±5	6
2	−0·9±0·6	5*	0·4±1·3	6	20±6	5*	51±10	6
3	−1·5±1·1	5*	2·7±0·5	6	21±7	5*	50±4	6
4	−0·6±0·8	4*	2·4±1·1	4	18±15	4*	45±4	4
5	−3·0±2·1	4*	2·9±0·7	4	23±11	4	49±2	4
6	−0·5±0·9	4*	1·9±1·9	4	30±10	4*	50±2	4
7	0·2±0·6	4	1·9±1·8	3	29±12	4*	46±2	3

Results are means ± s.e.m. **P*<0·05 Mann–Whitney *U* test

Mean resting energy expenditure (REE) was similar (placebo 104±1·7, BSHGH, 108±3·2 per cent control). These results demonstrate that during postoperative hyponitrogenous and hypocaloric intravenous nutrition, nitrogen balance becomes positive and fat oxidation is doubled with the administration of BSHGH.

Changes in hepatic haemodynamics with the development of liver metastases

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The ratio of the hepatic artery flow (HAF) to total liver blood flow measured by dynamic scintigraphy, the hepatic perfusion index (HPI), is reported to predict the presence of occult liver metastases in patients with colorectal carcinoma[1], but the mechanism of this phenomenon is unknown. The aim of this study was to determine the haemodynamic changes responsible for the alteration in the HPI with the development of micrometastases.

Metastases were induced by an intraportal injection of 8×10^7 Walker carcinosarcoma cells. Animals were studied 2, 4 and 6 days after inoculation. The HPI was measured by dynamic scintigraphy using an intraventricular bolus of 80 MBq of ^{99m}Tc sulphur colloid. HAF and portal venous inflow (PVI) were determined using the ^{57}Co microsphere technique. The presence of any intrahepatic arteriovenous shunting (HS) was determined after an hepatic artery injection of ^{99m}Tc labelled macro-aggregated albumin (40 μ).

Micrometastases were present 4 and 6 days after inoculation. The HPI at 4 days (51·80±1·68, *n*=16) and at 6 days (67·81±3·38, *n*=16) was significantly greater (*P*<0·001, Mann–Whitney *U* test) than in normal rats (33·78±1·77, *n*=20). HAF did not change with the development of metastases but PVI was significantly decreased at 6 days (*P*<0·001), and was associated with a significant increase in splanchnic vascular (SVR) and portal venous resistance (*P*<0·001). At 4 and 6 days after inoculation HS was also significantly increased (*P*<0·005).

These results indicate firstly, that the HPI alters with the development of micrometastases secondary to decreased PVI; and secondly, that the reduction in PVI is related to an elevation in hepatic vascular resistance consequent upon increased intrahepatic shunting.

1. Leveson SH, Wiggins PA, Giles GR, Parkin A, Robinson PJ. Deranged liver blood flow patterns in the detection of liver metastases. *Br J Surg* 1985; **72**: 128–30.

Evidence that transplanted hepatocytes retain functional activity in a model of liver injury

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Isolated rat hepatocytes, when transplanted into the spleen, survive for several months. If they also retained function, this technique may be of value in the treatment of liver disease. We have, therefore, examined whether hepatocytes transplanted into the spleens of animals with liver injury proliferate and improve hepatic function.

Chronic liver injury was induced in Lewis rats by a regimen of phenobarbitone and CCl$_4$ for 10 weeks followed by an end-to-side portcaval shunt. Transplanted animals received an intrasplenic injection of 10^7 hepatocytes isolated from the liver of normal Lewis donors. Antipyrine clearance was assessed at the time of transplantation (time 0) and at 4, 10 and 26 weeks by administering antipyrine intravenously (50 mg kg^{-1}) and measuring its concentration in saliva at 1, 2, 4, 8 and 24 h by HPLC.

	Antipyrine clearance (ml min^{-1} kg^{-1})		
Group	0	4 weeks	10 weeks
Liver injury only (controls)	4·1±0·2	1·7±0·7	2·2±0·5
Liver injury and hepatocyte transplantation	4·2±0·8	2·8±0·5	3·7±1·1
Mann–Whitney *U* test	n.s.	*P*<0·05	*P*<0·01

Results are means ± s.d.

Antipyrine clearance was normal in all animals before portacaval shunt. Thereafter, both groups showed reduced antipyrine clearance as liver injury progressed but, at both 4 and 10 weeks, antipyrine clearance was significantly greater in the transplanted group. This suggests that hepatocytes proliferate and may retain at least some functional activity after transplantation into recipients with severe liver injury.

Dynamics of bile flow through the human choledochal sphincter following exploration of the common bile duct

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Exploration of the common bile duct (CBD) and insertion of a T-tube is associated with a higher incidence of postoperative morbidity and mortality. Primary closure of the CBD has been advocated in patients who have choledochoscopic evidence of complete stone removal.

Using a system primed with the patient's own bile, the opening pressure and flow rate at maximal hepatic secretory pressure (30 cm bile) has been measured postoperatively in 17 patients undergoing CBD exploration. Only one patient had a negative exploration. In addition to manometric studies, bile biochemistry, bacteriology and viscosity were measured. The results (mean ± 95 per cent confidence limits) were as follows.

Day	Opening pressure (cm bile)	Flow rate(ml bile/min)
1	17·2±3·8	23·9± 7·7
2	15·2±2·9	26·5± 7·4
3	13·6±1·7	22·3± 5·5
4	10·4±1·8**	30·4± 7·6
5	9·4±1·8**	35·9±13·0
6	9·4±1·7**	34·9± 8·7*
7	9·1±1·8**	40·0±12·0**

* *P*<0·02; ***P*<0·01 (Wilcoxon signed rank sum)

The results show a temporary holdup at the choledochal sphincter which is independent of changes in bile viscosity and biochemistry. This is probably due to oedema. The pressure required to overcome the opening pressure on the first postoperative day, of 17·2 cm bile, indicates that primary closure of the CBD may be hazardous.

The effects of a long-acting analogue of somatostatin, SMS 201-995, on reticulo-endothelial system activity in the cirrhotic rat and on monocyte function in patients with cirrhosis

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We have recently demonstrated that a long-acting analogue of somatostatin, SMS 201-995, stimulates reticulo-endothelial system (RES) activity in the normal rat. The purpose of this study was to investigate the effects of SMS 201-995 on RES activity in rats with established cirrhosis and on peripheral monocyte function of cirrhotic patients with portal hypertension.

Male Wistar rats, with dimethylnitrosamine induced cirrhosis, received 2 μg SMS 201-995 b.d. subcutaneously for 7 days. A control group of cirrhotic rats were dosed similarly with saline. RES activity (uptake of ^{99m}Tc sulphur colloid by the liver and spleen) was measured on the eighth day after commencement of treatment with SMS 201-995 or saline.

Monocytes from 21 patients with cirrhosis and control subjects were prepared as previously described[1]. The effects of SMS 201-995 *in vitro* on monocyte function was assessed by the ability of the cells to phagocytose latex beads[1].

The liver-to-blood ($13{\cdot}7 \pm 2{\cdot}6$) and spleen to blood ($26{\cdot}5 \pm 3{\cdot}2$) ratios of ^{99m}Tc sulphur colloid in cirrhotic rats receiving SMS 201-995 were significantly greater ($P < 0{\cdot}01$) than those of animals treated with saline (liver-to-blood $2{\cdot}6 \pm 1{\cdot}2$, spleen to blood $13{\cdot}7 \pm 2{\cdot}8$). SMS 201-995 also significantly increased the phagocytosis of latex beads by monocytes from cirrhotic patients ($23{\cdot}5 \pm 2{\cdot}3$ to $42{\cdot}3 \pm 11{\cdot}1$ per cent; $P < 0{\cdot}0001$, Student's *t* test).

These results suggest that SMS 201-995 may stimulate both the RES system and peripheral monocytes, and may be of value in the management of patients with decompensated cirrhosis and impaired RES function.

1. Al-Sumidaie AM, Copeland GP, Leinster SJ, Jenkins SA. The effect of colorectal malignancies on monocyte migration, lysozyme production and phagocytosis. *Eur J Oncol* 1986; **12**: 367–71.

The effect of degradable starch microspheres (DSM) on hepatic blood flow for selective hepatic arterial chemotherapy

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The uptake of cytototic drugs by liver tumours after selective hepatic arterial infusion can be increased by simultaneous administration of degradable starch microspheres (DSM)[1]. However there are variable degrees of drug retention, partly due to the presence of abnormal arteriovenous (AV) shunts, which may have an influence on the efficacy of such treatment. This aspect was investigated in 11 studies on 6 patients receiving hepatic arterial chemotherapy via a Portacath® cannula. The optimum dose of DSM was measured by dynamic scintigraphy after an injection of ^{99m}Tc-labelled MAA (macro-aggregated albumin) before and after three consecutive injections of 300 mg DSM mixed with ^{99m}Tc-labelled HSA (human serum albumin) and given via the portacath.

Two indices were measured. Firstly, the percentage shunt index (PSI), which if greater than 1·0, reflects AV shunting. The median PSI was 1·35 (range 1·12–2·6). Secondly, the overall retention fraction (RF) which measures the percentage uptake of drug by the liver. The median RF was 0·15 (range 0·01–0·28). The values obtained from individual patients resulted in the optimal dose of DSM being reduced from 900 to 600 mg in three out of six patients.

In conclusion, the individual dosage requirements of DSM vary and the amount of drug retention by the liver is suboptimal due to the presence of AV shunts.

1. Flowerdew ADS, Britten AJ, Taylor I. The effect of degradable starch microspheres (DSM) on hepatic blood flow for selective hepatic arterial chemotherapy. *Gut* (in press).

Chronic exposure to dialysis fluid enhances peritoneal plasminogen activator activity (PAA)

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Despite recurrent attacks of peritonitis, patients undergoing continuous ambulatory peritoneal dialysis often remain free from peritoneal adhesions. The breakdown of fibrinous adhesions, which commonly form during peritonitis, and which may be converted into fibrous adhesions, is mediated by plasminogen activators secreted by peritoneal mesothelial cells[1].

Ten rats were given twice-daily intraperitoneal injections of 20 ml dialysis fluid for 6 weeks. In five rats the peritoneal PAA was estimated by measuring the area of lysis which developed around a layer of mesothelial cells after incubation on a plasminogen-rich fibrin plate for 24 h (reference 2). In the remainder, the number of mesothelial cells per unit area was counted by *en face* light microscopy. Control groups consisted of rats which had received no injections.

	Control ($n = 5$)	Experimental ($n = 5$)	Mann–Whitney *U* test
Lytic area (mm^2)	71 (64–78)	99 (91–108)	$P = 0{\cdot}008$
Cells per mm^2	2100 (1300–2300)	3440 (3100–4200)	$P = 0{\cdot}008$

The median and range values are given

Mesothelial hyperplasia occurs after chronic exposure to dialysis fluids and is associated with enhanced peritoneal PAA. Peritoneal dialysis may be a useful adjunct to surgical lysis in patients with recurrent intraperitoneal adhesions.

1. Buckman RF, Buckman PD, Hufnagel HV, Gervin AS. A physiologic basis for the adhesion free healing of deperitonealized surfaces. *J Surg Res* 1976; **21**: 67–76.
2. Raftery AT. A method for measuring fibrinolytic activity in a single layer of cells. *J Clin Pathol* 1981; **34**: 625–9.

Prosthetic materials in abdominal wall reconstruction

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Prosthetic materials are increasingly used for the repair of incisional hernias and abdominal wall defects. The most frequent site for failure is at the edge of the prosthetic material[1].

We have investigated the use of polypropylene mesh (PPM), expanded polytetrafluorethylene patch (PTFE) and polyglycolic acid mesh (PGA) for abdominal wall reconstruction in rats. The strength of the interface between the prosthetic material and the abdominal wall muscle was recorded using a tensiometer.

There was no significant difference in wound strength between PPM and PTFE repaired defects. However, after PGA is absorbed, wounds repaired with PPM or PTFE become significantly stronger ($P < 0{\cdot}05$).

Table *Wound strength (N/cm)*

	Overlap between prosthetic material and muscle (mm)		
	2	4	6
PPM	$15{\cdot}4 \pm 3{\cdot}9$	$17{\cdot}6 \pm 4{\cdot}0$	$19{\cdot}3 \pm 3{\cdot}8$*
PTFE	$11{\cdot}9 \pm 2{\cdot}5$	$14{\cdot}8 \pm 3{\cdot}4$	$19{\cdot}2 \pm 5{\cdot}3$**

All results are means ± s.e.m. Between 2 and 6 mm overlap, *$P < 0{\cdot}05$; **$P < 0{\cdot}01$ (Mann–Whitney *U* test)

A greater overlap between the prosthetic materials and the abdominal muscles significantly increased the strength of the repair.

Histological assessment of PTFE shows a uniform cellular and collagen ingrowth into the interstices of the material, while PPM is incorporated by irregular dense collagen fibres. The peritoneal surface of PTFE alone supports a mesothelial like layer, confirmed by electron microscopy.

PGA is an unsuitable material for permanent repair of abdominal wall defects. PPM and PTFE support a strong repair with sufficient tissue overlap, but PTFE is more uniformly incorporated into tissues which produces a more supple wound.

1. Lewis RT. Knitted polypropylene mesh in the repair of incisional hernias. *Can J Surg* 1984; **27**: 155–7.

Endotoxin handling after acute liver injury

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Circulating endotoxins are normally removed by the liver. However, in acute liver failure, endotoxin clearance may be depressed and may contribute to hepatorenal failure. A model of acute liver damage has been developed to permit the study of endotoxin handling.

Male Wistar rats received galactosamine 1 mg/g in saline IP ($n = 7$), or 2·5 ml saline ($n = 9$). After 24 h, chromium labelled endotoxin was given intravenously and its rate of clearance from the blood measured. The anaesthetized animals were killed at 1 h, and tissue uptake of endotoxin was measured by gamma counting.

Endotoxin clearance in saline treated rats was bi-exponential with a mean fast component slope of $5{\cdot}32 \times 10^{-3}$ cpm/min (s.e.m. $0{\cdot}30 \times 10^{-3}$ cpm/min). Treated animals cleared endotoxin more slowly, and mono-exponentially ($2{\cdot}10 \times 10^{-3}$ cpm/min, s.e.m. $0{\cdot}602 \times 10^{-3}$ cpm/min, $P = 0{\cdot}007$).

After galactosamine, the liver contained significantly lower levels of endotoxin, but the kidneys took up significantly more. Uptake of ^{51}Cr-labelled endotoxin by the organs was as follows.

	Kidney	Liver	Spleen	Heart
Galactosamine	1·52 (0·34)	2·23 (0·49)	2·41 (0·49)	0·13 (0·04)
Controls	0·45 (0·07)	4·68 (0·53)	4·03 (0·70)	0·11 (0·03)
P	$<0·005$	$<0·03$	n.s.	n.s.

The values are means (and s.e.m.) calculated as a percentage of the injected dose of labelled endotoxin per gram of tissue

The acute liver injury of galactosamine is a satisfactory model for the study of endotoxin handling and may provide a means of investigating protective agents.

Impaired clearance of circulating macromolecular enzyme inhibitor complexes in severe acute pancreatitis—an important aspect of pathogenesis?

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Trypsin liberated in plasma is rapidly complexed with α_2-macroglobulin (α_2-M) and cleared by the reticulo-endothelial system (RES), with a half-life of 8–10 min in normal individuals[1]. Enzyme–α_2-M complexes possess peptidase activity, and imbalance of complexed 'fre α_2-M' leads to fatal shock in experimental animals[2]. In severe acute pancreatitis (AP) α_2-M levels fall, and up to 30 per cent of plasma α_2-M is present as complexes, suggesting grossly delayed clearance by the RES. The clearance of trypsin–α_2-M complexes from plasma was studied in three normal controls and nine patients with AP (five mild, four severe, according to clinical criteria) on the day of admission to hospital. After taking a baseline blood sample, 1 mg ^{14}C-trypsin (specific activity 370 kBq/mg) was injected intravenously. Blood samples were collected immediately, at 1 min intervals for 20 min, and at 2 min intervals for a further 20 min. Radioactivity was counted by liquid scintillation, and the plasma ^{14}C-trypsin–α_2-M half-life ($t_{\frac{1}{2}}$) calculated as time to 50 per cent reduction of initial activity.

		Plasma ^{14}C-trypsin–α_2-M $t_{\frac{1}{2}}$ (min)	
	n	Median	Range
Normal	3	10·5	8·1–11·7
Mild	5	9·7	4·8–26·8
Severe	4	21·6	17·7–31·0*

* Severe AP group significantly different from the normal group, $P<0·05$ (two-sample rank test)

This study demonstrates, for the first time, delayed clearance of trypsin–inhibitor complexes from the plasma of patients with AP and suggests that investigative emphasis should be placed upon the significance of circulating macromolecular complexes, and not solely upon enzyme–substrate relationships.

1. Ohlsson K, Laurell C-B. The disappearance of enzyme inhibitor complexes from the circulation of man. *Clin Sci Mol Med* 1976; **51**: 87–92.
2. Ohlsson K. Experimental pancreatitis in the dog. Appearances of complexes between proteases and trypsin inhibitors in ascitic fluid, lymph and plasma. *Scand J Gastroenterol* 1971; **6**: 645–52.

Peritoneal fluid enzymes and antiproteases in acute pancreatitis

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In experimental canine pancreatitis, saturation of peritoneal α_2-macroglobulin (α_2-M) by proteases is followed by activation of trypsinogen, saturation of α_1-antiprotease (α_1-AP), hypotension and death[1]. We have analysed peritoneal fluid samples from 19 patients for tryptic amidase activity, trypsin binding capacity, free proteolytic activity, amylase, lipase, protein, α_2-M and α_1-AP. A total of 10 patients had free peritoneal fluid and all 19 had return fluids studied after a 1 litre saline lavage. After lavage aprotinin (5 × 10^6 kilounits in 1 litre of saline) was instilled and return fluids studied 8 h later.

	Free fluid ($n=10$)	Fluid after saline lavage ($n=19$)	Fluid 8 h after aprotinin ($n=18$)
Protein (g/l)	44·7 ± 7·1	3·8 ± 2·4	9·3 ± 5·2
Amylase (units/l)	25 000 ± 12 621	3566 ± 3298	9227 ± 6213
Lipase (units/l)	29 529 ± 14 271	4043 ± 3971	8447 ± 7659
Tryptic amidase ($\Delta A_{405\,nm}$/60 min)	0·245 ± 0·203	0·016 ± 0·017	0·004 ± 0·007

Results expressed as mean ± s.d.

Free fluids showed high pancreatic enzyme activity and the increased activity in return fluids between the saline lavage and aprotinin 8 h later indicate continued enzyme release. Free proteolytic activity was not found, although five of seven free fluids showed high tryptic amidase activity representing trypsin–α_2-M complexes. Trypsin binding capacity was reduced but not exhausted in five of nine free fluids, but continuing enzyme release may pose a threat should α_2-M and α_1-AP become saturated. Three fatal cases had low peritoneal α_2-M. Washout of the peritoneal cavity and instillation of aprotinin effectively eliminates tryptic amidase activity and seems a logical therapeutic approach which is currently under study.

1. Ohlsson K, Tegner H. Experimental pancreatitis in the dog. Demonstration of trypsin in ascitic fluid, lymph and plasma. *Scand J Gastroenterol* 1973; **8**: 129–33.

Treatment of experimental acute necrotizing haemorrhagic pancreatitis by whole blood exchange transfusion

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No specific treatment exists for acute haemorrhagic pancreatitis (AHP), for which the mortality is 75 per cent. Exchange transfusion (XT), which offers a means of clearing toxins from the circulation, has been investigated.

In the male Sprague–Dawley rat, AHP was induced by transduodenal cannulation of the bile–pancreatic duct and infusion of a bile salt/lysolecithin mixture. AHP ensued with the development of blood-stained ascites and a rapid rise in serum amylase. XT was performed using 15 × 1 ml aliquots of donor rat blood. An exchange efficiency of 70 per cent was obtained as assessed with radiolabelled serum albumin. All animals were monitored until death or killing at 72 h. In 20 untreated animals, the mortality at 24 h was 60 per cent and at 72 h 90 per cent. In 20 animals, XT at 1 h reduced the mortality to 10 and 20 per cent respectively ($\chi^2=10·99$, $P<0·0001$ and $\chi^2=19·8$. $P<0·0001$). The 72 h mortality if XT was carried out at 2 or 4 h was 67 and 87 per cent (n.s.). The administration of fresh plasma 1 h after induction of AHP did not reduce the mortality.

XT can reduce the mortality from experimental AHP to low levels if it is carried out early in the disease process. In man, expeditious XT may reduce the mortality of AHP.

Short notes

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Morbidity after surgery for breast cancer

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The late sequelae of mastectomy are well recognized[1]. These include frozen shoulder, damage to the intercostobrachial nerve, chest wall pain and arm lymphoedema. We studied whether more conservative surgery results in the same incidence of morbidity by means of a questionnaire.

Patients and methods

Between January 1981 and December 1983 172 consecutive patients had surgery for carcinoma of the breast in one surgical unit. At the time of the questionnaire in May 1986, 17 patients had died and we were unable to trace 47 patients. 108 questionnaires were sent, with 97 replies. The notes of these patients were also reviewed. Peripheral tumours less than 3 cm were treated by local excision, axillary sampling and radical radiotherapy. Central tumours and those larger than 3 cm were treated by simple mastectomy, axillary node sampling and, if node positive, by radiotherapy. Radical radiotherapy comprised 30 fractions giving 5000 cGy to the breast and node areas and 1000 cGy to the tumour site. Sampling of the axilla consisted of removal of those nodes adjacent to the axillary tail only. Of the 97 patients, 32 had lumpectomy and 65 mastectomy.

The questionnaire concentrated on four main areas: frozen shoulder, intercostobrachial nerve damage, chest wall or breast pain and arm lymphoedema. The patients were asked about immediate complications and pain in the chest wall or breast, shoulder or arm and asked to grade this on a linear analogue scale and to describe the course of the problem and its duration. Similarly they were asked about abnormal sensations and swelling of the arm. The questions were deliberately kept simple and space provided for elaboration by the patient to encourage a high return.

Results (*Table 1*)

The mean age and standard deviation of the lumpectomy group was 60±12 years compared with 65±12 years for the mastectomy group. Tumour stage was earlier in the lumpectomy group, in that 50 per cent were in stage 1 compared with 20 per cent for the mastectomy group. Overall complication rates were: wound infection, defined as that requiring either antibiotic therapy or drainage, 7 per cent; seroma formation, defined as a fluid collection requiring aspiration, 2 per cent; flap necrosis, defined as visible skin necrosis, 3 per cent and haematoma, defined as that requiring aspiration or evacuation, 3 per cent. There was one locoregional recurrence, which was in the mastectomy group. Of the mastectomy patients 43 (66 per cent) required radiotherapy and 51 per cent of the complications after mastectomy were in patients receiving radiotherapy. Eleven (34 per cent) patients in the lumpectomy group did not complain of symptoms compared with 32 (49 per cent) in the mastectomy group. In the mastectomy patients 3 (4·6 per cent) complained of more than one symptom compared with 7 (22 per cent) of lumpectomy patients. All complaints were prolonged, frozen shoulder having the shortest duration: 2–3 months in 88 per cent of patients. Intercostobrachial nerve damage was evidenced by paraesthesia or anaesthesia in the distribution of the nerve, 87 per cent of patients having symptoms for 1 year to 18 months. Breast pain occurred as tenderness or sudden sharp stabbing pains and was persistent. Arm lymphoedema was only assessed subjectively, 25 per cent of patients having a severe problem. The results of the sequelae after surgery are tabulated below. None of the differences between the two groups achieved statistical significance using the χ^2 test.

Table 1 *Sequelae after surgery*

	Frozen shoulder	Intercostobrachial nerve damage	Chest wall/ breast pain	Arm lymphoedema
Lumpectomy	7 (22%)	6 (19%)	8 (25%)	6 (19%)
Mastectomy/ RT	4	6	5	4
Mastectomy/ No RT	5	11	2	2
Mastectomy/ Total	9 (14%)	17 (26%)	7 (11%)	6 (9%)

Values are numbers of patients with percentage incidence in parentheses

Discussion

Survival of patients with carcinoma of the breast has not been altered by the type of surgery performed. Therefore the effects of body image and morbidity following surgery become relatively more important. The lumpectomy group had as many problems as the mastectomy group, but all patients had node sampling of the axilla and radical radiotherapy. Previous studies have shown that radiotherapy and surgery on the axilla combine to cause increased problems of movement at the shoulder and intercostobrachial nerve damage[1]. The incidence of arm lymphoedema is similar for all types of procedure on the axilla unless clearance is combined with radiotherapy when it increases fourfold[2]. Breast pain may be caused by fibrosis following radiotherapy together with surgical scarring. All the problems seen were prolonged and caused considerable morbidity, and frequently the patients regarded the persistence of such symptoms as evidence that the cancer was still present.

Little can be done about the harmful effects of radiotherapy apart from greater fractionation but there is recent evidence that careful preservation of the intercostobrachial nerve during axillary dissection decreases the incidence of postoperative paraesthesia and anaesthesia without increasing local recurrence[3]. This survey has shown that problems following mastectomy were equalled by those for lumpectomy and confirms the adverse combination of radiotherapy and surgery on the axilla found by other studies[1,2,4].

References

1. Aitken DR, Minton JP. Complications associated with mastectomy. *Surg Clin N Am* 1983; **63**: 1331–52.
2. Kissin MW, Quercy G, Easton D, Westbery G. Risk of lymphoedema following treatment of breast cancer. *Br J Surg* 1986; **73**: 580–4.
3. Temple WJ, Ketchman AS. Preservation of the intercostobrachial nerve during axillary dissection for breast cancer. *Am J Surg* 1985; **150**: 585–8.
4. Mazeron JJ, Otmezguine Y, Huart J, Pierquin B. Conservative treatment of breast cancer: results of management of the axillary lymph node area in 3353 patients. *Lancet* 1985; **i**: 1387.

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Lymph nodes presenting as breast lumps

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Enlarged lymph nodes presenting as palpable breast lumps have usually been reported in association with a skin disease e.g. psoriasis[1,2]. Here we report a 6 year experience of 18 patients with such breast lumps seen at Charing Cross Hospital. Only one of these patients had an associated skin disease.

Methods

The records of all patients with a histological diagnosis of intramammary lymph node who presented to the Breast Unit, Charing Cross Hospital within the 6 year period 1981–1986 were reviewed. Patients with axillary lymphadenopathy were excluded. The relevant patient data were collated, and all microscopic slides were reviewed.

Results

Eighteen patients with nineteen breast lumps (one bilateral) were identified. Their ages ranged between 22 and 58 years (mean 32·6 years). One patient was postmenopausal. The length of history varied between 1 and 36 months (mean 5·9 months). The lumps were painful in three patients (16·6 per cent). One patient had a history of previous ipsilateral breast biopsy for fibrocystic change. Four patients (22·2 per cent) were taking the contraceptive pill.

On examination all nodes were superficial and mobile. Of 19 lumps 13 (68·4 per cent) were present toward the periphery of the breast and 6 (31·6 per cent) were in the upper outer quadrant (*Figure 1*). In this series there was no evidence of lymphadenopathy elsewhere. Only one patient had a skin disease (*lichen planus*).

The pre-operative diagnosis was of fibro-adenoma in six (31·5 per cent), cysts in four (21 per cent) and unspecified lump in five cases (26·3 per cent). The correct diagnosis of lymph node was made in four cases (21 per cent).

Routine haematology and chest X-ray, where done, were normal. All patients were treated by excision biopsy. Aspiration cytology was not performed. Follow-up varied from 1 month to 3 years (mean 8·1 months). One patient had a recurrent prominent lymph node at the site of the original biopsy 12 months after surgery. The patients' young age precluded mammography in most instances; where done, however, they were reported as normal.

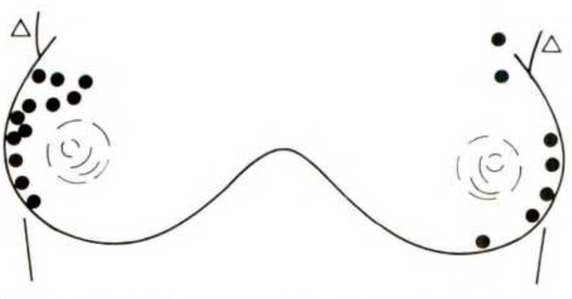

Figure 1 *The site of nineteen lymph nodes presenting as breast lumps in eighteen patients (excluding axillary tail)*

Pathology

The number of lymph nodes in each breast lump varied between one and six. Their mean diameter was 0·8 cm. Histological changes present included fibrosis, mostly hilar, in eleven cases (57 per cent), lymphoid hyperplasia in ten (52 per cent), sinus histiocytosis in seven (36 per cent), melanin pigmentation in seven (36 per cent) and fatty infiltration in four (21 per cent). A capsular naevus was seen in one lymph node (*Figure 2*).

Discussion

The majority of lymph nodes seen in this study (68·4 per cent) were situated superficially toward the periphery of the breast. Anatomically they probably belong to the external mammary lymph node chain[3]. Normally these nodes are not palpable, and account for less than 5 per cent of the total axillary drainage complement[3,4]. The remaining nodes were in the upper outer quadrant and probably belong to the prepectoral group[4].

In previous studies most patients have had an associated skin disease, e.g. eczema or psoriasis, with features of dermatopathic

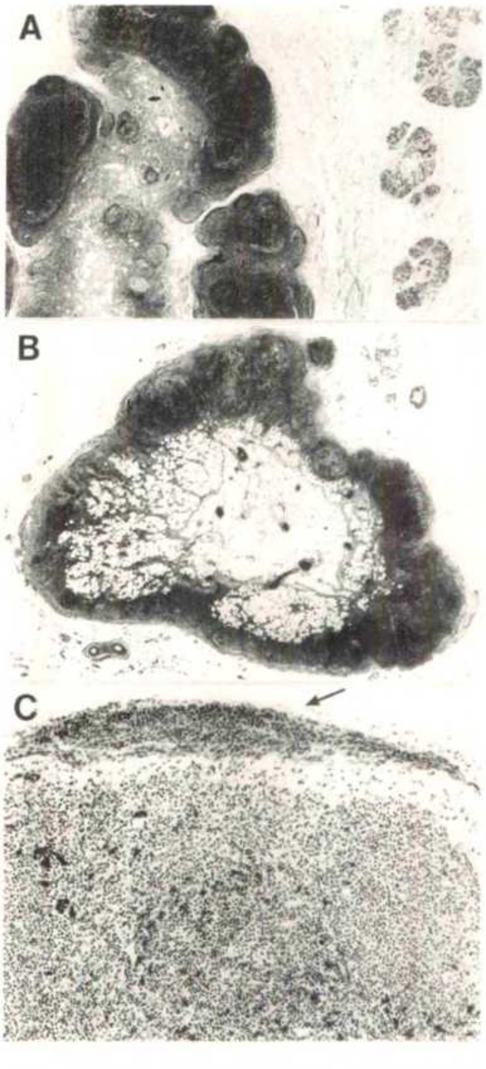

Figure 2 **A**. *A group of enlarged lymph nodes, showing reactive hyperplasia (haematoxylin and eosin × 12).* **B**. *An enlarged lymph node showing marked fatty infiltration corresponding to the 'doughnut' sign as seen on mammography (haematoxylin and eosin × 12).* **C**. *A capsular naevus (arrow) seen in an enlarged lymph node. The scattered darkly stained cells within the lymph node are dendritic and melanin containing cells. Immunoperoxidase for S100 (× 100)*

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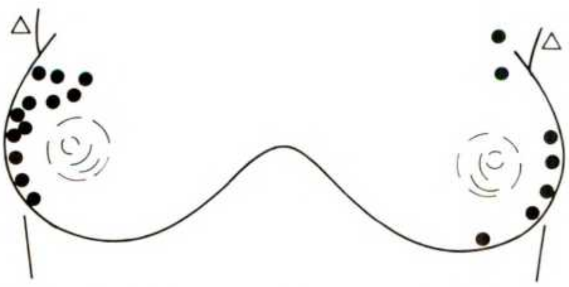

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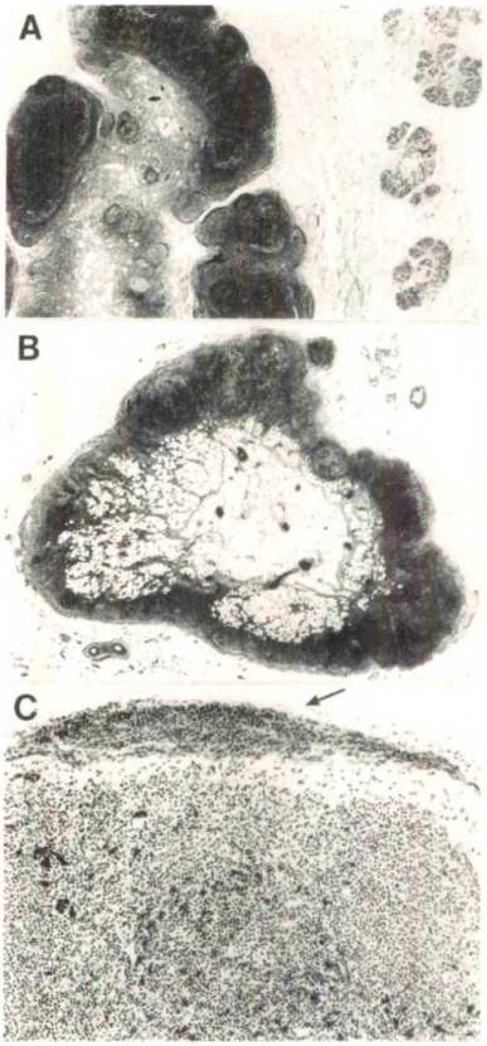

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lymphadenopathy in the involved lymph nodes[1,2]. Although many nodes in our study showed reactive changes and melanin pigmentation, features which usually suggest a skin disease—associated lymphadenopathy; only one patient had clinical evidence of this (*lichen planus*). We believe, therefore, that these nodes may become palpable in some patients without an obvious skin disease. It would be difficult to speculate about aetiology of the lymph node prominence in such patients, but the presence of melanin pigments and reactive hyperplasia raises the possibility of repeated minimal trauma particularly to the nipple or areola.

Intramammary lymph nodes may be detected on mammograms by the 'doughnut' sign, where fatty replacement at the hilum gives rise to an area of translucency or ring appearance[5]. As fatty infiltration was present in only 21 per cent of our cases (*Figure 2B*), mammography would not have aided diagnosis in most of these patients.

Acknowledgements

We wish to thank Susan Ellis for typing this manuscript.

References

1. Heymann AD, Rotterdam HZ. Dermatopathic lymphadenitis presenting as lateral breast mass. *JAMA* 1978; **240:** 1622–3.
2. Kopans DB, Meyer JE, Murphy GF. Benign lymph nodes associated with dermatitis presenting as breast masses. *Radiology* 1980; **137:** 15–19.
3. Haagensen CD. *Diseases of the Breast*. Philadelphia: W. B. Saunders Co., 1972: 35–6.
4. Rouvière, H. Anatomie des lymphatiques de l'homme. Paris: Masson, 1932.
5. Seymour EQ, Stanley JM. Intramammary lymph nodes: the 'doughnut' sign on mammography. *Breast* 1982; **8:** 26–7.

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Treatment of breast lumps in the teenager

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The presence of a breast lump in any age group raises the fear of malignancy, and as a result it has been suggested that all solid discrete lesions in the breast should be excised[1]. However, carcinoma is rare under 30 years of age and in one report no malignancy occurred under age 27 years[2]. If the risk of malignancy is negligible, a conservative attitude may be considered in teenage patients with breast lumps. To decide if this approach is appropriate, we analysed all our breast biopsies in the 13–19 age group.

Patients and methods

We reviewed all breast biopsies at the Port of Spain General Hospital in female patients between 13 and 19 years old over the 7-year period from 1976 to 1982.

Results

Of 2642 consecutive breast biopsies performed, 658 (24·9 per cent) were in teenage girls. In this group fibroadenoma occurred most frequently (77·6 per cent) and, with fibrocystic disease, accounted for 97 per cent of teenage breast lumps; no cases of carcinoma were encountered (*Table 1*). Of our patients with fibroadenoma, 14 per cent either had undergone previous excision of a fibroadenoma or returned with recurrence during the study period. Of the 2642 breast biopsies, 529 were malignant, the youngest 2 women being 23 and 25 years.

Table 1 *Histological diagnosis of breast biopsies in age group 13–19 years*

Fibroadenoma	511 (77·6)
Fibrocystic disease	130 (19·8)
Abscesses	14 (2·1)
Fat necrosis	1 (0·2)
Granular cell tumour	2 (0·3)

Figures in parentheses are percentages

Discussion

As in other series[1,2] there were no malignant lumps in our teenagers. The majority of breast lesions were fibroadenomas; these occur more commonly and at an earlier age in our population, whereas fibrocystic disease (the commonest differential diagnosis) increases with age. The clinical diagnostic accuracy for fibroadenoma in all ages can be as low as 50 per cent[1]. However, in our teenage population the diagnostic accuracy is very high (92 per cent) because fibroadenomas occur very frequently in coloured races and the diagnosis can be made with more certainty in this young age group where fibroadenosis is uncommon and carcinoma is very rare. In the 8 per cent misdiagnosed, the histological diagnosis was always benign, usually fibroadenosis.

Although the growth rate of fibroadenomas may increase in pregnancy, and in adolescence a large size may be reached, growth is slow and often self-limiting; thus surgery can be delayed in most patients. Fibroadenomas are often multiple and after early excision 10–20 per cent of patients return with more fibroadenomas[3]. Most of these recurrences occur within 5 years of surgery. Therefore, an aggressive surgical policy will result in multiple operations in a significant proportion of patients, whereas observation could result in a single operation for multiple fiboadenomas. Spontaneous regression has been reported in 10 per cent of fibroadenomas[4] and thus surgery may be avoided if an observation policy is instituted for teenage breast lumps. Malignant change within fibroadenomas is very rare, occurring on average 10 years after the mean age of women with fibroadenomas[5]; none of our cases showed evidence of carcinoma. The risk of a missed malignancy, or one arising in a fibroadenoma under observation, is minimal.

Fibrocystic disease, the next common cause of a breast lump, is best managed conservatively.

A conservative approach is now advised in the teenager, and fibroadenomas are now observed for 5 years before considering biopsy.

References

1. Williamson S, Forrest APM. Fibroadenoma of the breast. *Br J Surg* 1985; **72**: 838–40.
2. Ellis H, Cox PJ. Breast problems in 1000 consecutive referrals to surgical out-patients. *Postgrad Med J* 1984; **60**: 653–5.
3. Haagensen CD. *Diseases of the Breast*. 2nd ed. Philadelphia: W. B. Saunders, 1971: 214.
4. Furnival CM, Irwin JRM, Gray GM. Breast disease in young women—when is biopsy indicated? *Med J Aust* 1983; **2**: 167–9.
5. Pick PW, Ioulias A, Iossifides A. Occurrence of breast carcinoma within a fibroadenoma. *Arch Path Lab Med* 1984; **108**: 590–4.

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Lymph nodes presenting as breast lumps

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On examination all nodes were superficial and mobile. Of 19 lumps 13 (68·4 per cent) were present toward the periphery of the breast and 6 (31·6 per cent) were in the upper outer quadrant (*Figure 1*). In this series there was no evidence of lymphadenopathy elsewhere. Only one patient had a skin disease (*lichen planus*).

The pre-operative diagnosis was of fibro-adenoma in six (31·5 per cent), cysts in four (21 per cent) and unspecified lump in five cases (26·3 per cent). The correct diagnosis of lymph node was made in four cases (21 per cent).

Routine haematology and chest X-ray, where done, were normal. All patients were treated by excision biopsy. Aspiration cytology was not performed. Follow-up varied from 1 month to 3 years (mean 8·1 months). One patient had a recurrent prominent lymph node at the site of the original biopsy 12 months after surgery. The patients' young age precluded mammography in most instances; where done, however, they were reported as normal.

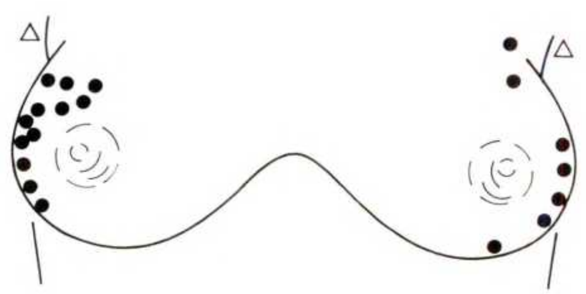

Figure 1 *The site of nineteen lymph nodes presenting as breast lumps in eighteen patients (excluding axillary tail)*

Pathology

The number of lymph nodes in each breast lump varied between one and six. Their mean diameter was 0·8 cm. Histological changes present included fibrosis, mostly hilar, in eleven cases (57 per cent), lymphoid hyperplasia in ten (52 per cent), sinus histiocytosis in seven (36 per cent), melanin pigmentation in seven (36 per cent) and fatty infiltration in four (21 per cent). A capsular naevus was seen in one lymph node (*Figure 2*).

Discussion

The majority of lymph nodes seen in this study (68·4 per cent) were situated superficially toward the periphery of the breast. Anatomically they probably belong to the external mammary lymph node chain[3]. Normally these nodes are not palpable, and account for less than 5 per cent of the total axillary drainage complement[3,4]. The remaining nodes were in the upper outer quadrant and probably belong to the prepectoral group[4].

In previous studies most patients have had an associated skin disease, e.g. eczema or psoriasis, with features of dermatopathic

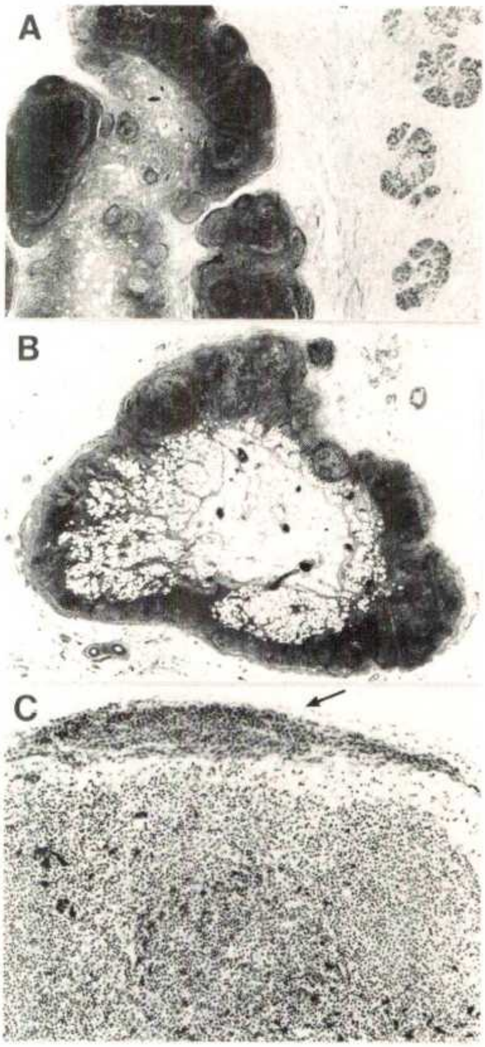

Figure 2 **A**, *A group of enlarged lymph nodes, showing reactive hyperplasia (haematoxylin and eosin × 12).* **B**, *An enlarged lymph node showing marked fatty infiltration corresponding to the 'doughnut' sign as seen on mammography (haematoxylin and eosin × 12).* **C**, *A capsular naevus (arrow) seen in an enlarged lymph node. The scattered darkly stained cells within the lymph node are dendritic and melanin containing cells. Immunoperoxidase for S100 (× 100)*

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Splenectomy as primary treatment for hairy cell leukaemia

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Hairy cell leukaemia is a lymphoproliferative disorder in which the tumour cells have monocytoid features on ultrastructural study[1]. However, the majority of the neoplasms are phenotypically mature B lymphocytes[2] and in addition express immunoglobulin gene rearrangement[3] although a T cell subset has been described[4–6]. The predominant features are moderate pancytopenia, although 20 per cent of the patients have white cell counts greater than 10×10^9/l; there is a lymphocytosis in which the cells show irregular cytoplasmic projections, giving rise to the term 'hairy' cells, and in leukaemic variants may account for more than 50 per cent of the differential count[7,8].

Treatment has not been defined by controlled study but a number of options are available[9]. Since approximately 90 per cent of patients ultimately require intervention it is noteworthy that splenectomy is not only of value in those with haematological deterioration or symptoms attributable to splenic enlargement, but is also frequently effective even with minimal splenomegaly and the response rate does not correlate with spleen weight[10,11]. Although haematological values may return to normal in approximately 40 per cent of patients[12] atypical cells persist in the peripheral blood and marrow. In patients where disease progression occurs after splenectomy, treatment with chlorambucil for prolonged periods of time is reported to be beneficial[12]. More recently, interferon has emerged as an alternative and apparently highly successful therapeutic option[13] and, similarly, pentostatin may have a role perhaps even before splenectomy[14].

Many of these features, and particularly the benefit of splenectomy are illustrated by recent experience with 10 patients.

Patients and methods

All patients had a history taken and underwent physical examination, after which baseline haematology was determined using the Coulter Counter Model S-Plus, biochemical profile was established, bone marrow was assessed using aspiration and trephine biopsy techniques and spleen size were documented by radionuclide scanning (*Table 1*). A surgeon with an interest in haematological malignancy carried out the splenectomy using a meticulous haemostatic technique. Postsplenectomy haematological values were monitored serially.

Results (*Table 1*)

Seven of the ten patients are alive 3–7 years after splenectomy.

Discussion

Hairy cell leukaemia, or leukaemic reticulo-endotheliosis, was described as a distinct clinicopathological entity more than a quarter of a century ago[15] and has attracted interest for two major reasons. First is the ease with which the clinical presentation and the haematological findings, including cytochemistry and ultrastructure, can be confused with a B cell lymphoma[16,17]. In this regard the common clinical presentation of pancytopenia in the absence of significant peripheral lymphadenopathy, usually occurring in the middle-aged man with massive splenomegaly, may arise with both hairy cell and pseudo-hairy cell leukaemia[16–18]. In both of these entities an accurate diagnosis is necessary as a basis for treatment and histopathology of the spleen has been found most reliable in this regard[16], although immunophenotyping using monoclonal antibodies may also be helpful[2].

Secondly, the approach to management of leukaemic reticulo-endotheliosis is different from that of the superficially similar B cell lymphoma so that it is of practical importance to make this distinction. Patients with pseudo-hairy cell leukaemia follow a different clinical course from those with leukaemic reticulo-endotheliosis, usually requiring therapy at an earlier stage. In contrast, splenectomy alone[19] is frequently the only intervention required in those with true hairy cell leukaemia, and our current experience is consistent with this reported recommendation[10,11,19–22].

A further point of practical management is that the use of interferon[13,23] is especially effective in patients with this entity. It is not yet established whether interferon is optimally beneficial without splenectomy but the oncological precedent of bulk reduction of a tumour before treatment, wherever practical, would seem a sensible approach, particularly where this operation may alone confer a lasting benefit.

Typically, pancytopenia is improved by splenectomy in these patients. However, in two of the present series a rather atypical response was documented. Thus, in patient 7, while red cell transfusion was abolished, there was a poor response in neutrophil count and, paradoxically, platelet count fell. Similarly, in patient 9 the platelet count showed a consistent fall after removal of the spleen. The explanation for this observation is unknown and it can only be speculated that removal of the spleen may have deprived these two individuals of areas of extramedullary haematopoiesis that contributed significantly to platelet production.

Patients with hairy cell leukaemia have a predisposition to infection, which might theoretically be aggravated by splenectomy. Death in one of the three patients who died was due to overwhelming sepsis despite prior immunization with pneumococcal vaccine and appropriate intravenous antibiotics. In the other two it was not possible to establish the cause of death, but in neither was there any reason to believe that infection contributed. Nevertheless, it would seem prudent to vaccinate patients undergoing splenectomy with a polyvalent pneumococcal vaccine. It has not been our practice to administer long-term prophylactic antibiotics, and this issue remains controversial.

The present experience confirms the benefit of splenectomy as the initial form of treatment for patients with hairy cell leukaemia since prolonged periods of clinical and haematological stability may avert the need for further treatment[24]. Furthermore, the availability of splenic histopathology facilitates the distinction between hairy cell leukaemia and the superficially similar B-lymphocytic lymphoma. In the latter, conventional treatment with alkylating agents may be needed, whereas in the former the use of these drugs is best avoided, and here interferon holds out promise for obtaining a response in a substantial number of individuals[25].

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Table 1 *Clinical and haematological findings**

				Presplenectomy			Postsplenectomy			
Patient	Age	Sex	Clinical presentation	Hb (g/dl)	WBC ($\times 10^9$/l)	Platelets ($\times 10^9$/l)	Hb (g/dl)	WBC ($\times 10^9$/l)	Platelets ($\times 10^9$/l)	Postsplenectomy status
1	70	F	12 cm splenomegaly Skin infiltration Recurrent infections	7·4	8·5	75	10·8	4·0	190	Alive and well at 5 years
2	68	F	18 cm splenomegaly	8·9	3·8	126	11·0	8·5	401	Died at 4 months Cause unknown
3	65	F	18 cm splenomegaly	6·0	3·8	45	12·0	10·3	277	Alive and well at 3 years Transfusion requirement abolished
4	43	M	21 cm splenomegaly Swollen left leg	7·1	20·5	120	NA†	NA	NA	Died postoperatively Unanticipated overwhelming sepsis Autopsy refused
5	49	M	19 cm splenomegaly	14·1	4·8	117	15·6	7·3	281	Alive and well at 4 years
6	48	M	4 cm splenomegaly Recurrent chest infections	8·5	2·5	60–75	12·8	5·9	240	Alive and well at 5 years Transfusion requirement abolished
7	69	M	10 cm splenomegaly	4·5	1·3	500	12·0	1·5	150	Died at 18 months Cause unknown Autopsy refused
8	43	F	10 cm splenomegaly	10·0	4·5	140	13·2	6·0	200	Alive and well at 7 years
9	76	F	15 cm splenomegaly	12·1	11·8	527	10·8	1·9	188	Alive and well at 4 years
10	58	M	4 cm splenomegaly Thrombocytopenic purpura Asymptomatic haemochromatosis	10·7	1·0	50	12·8	9·0	387	Alive and well at 5 years Transfusion requirement abolished Postoperative rise in white cell count controlled with interferon

* Of the three patients who died infection was not considered a contributing cause in two cases (cases 2 and 7), whereas in one (case 4) this was due to unanticipated overwhelming sepsis despite pre-operative immunization with polyvalent pneumococcal vaccine

† NA, not available

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References

1. Golomb HM, Braylan R, Polliack A. 'Hairy' cell leukaemia (leukaemic reticuloendotheliosis): a scanning microscopic study of eight cases. *Br J Haematol* 1975; **29**: 455–60.
2. Tubbs RR, Savage RA, Sebek BAS, Fishleder A, Weick JK. Antigenic phenotype of splenic hairy cells. *Am J Med* 1984; **76**: 199–205.
3. Cleary ML, Wood GS, Warnke R, Chao J, Sklar J. Immunoglobulin gene rearrangements in hairy cell leukaemia. *Blood* 1984; **64**: 99–104.
4. Hernandez D, Cruz C, Carnot J, Borticas E, Espinosa E. Hairy cell leukaemia of T cell origin. *Br J Haematol* 1978; **40**: 504–6.
5. Saxon A, Stevens RH, Golde DW. T-lymphocyte variant of hairy-cell leukaemia. *Ann Intern Med* 1978; **88**: 323–6.
6. Worman CP, Cawley JC. Monoclonal antibody-defined T-cell subsets in hairy-cell leukaemia. *Scand J Haematol* 1982; **29**: 338–44.
7. Golomb HM, Catovsky D, Golde DW. Hairy cell leukemia. A clinical review based on 71 cases. *Ann Intern Med* 1978; **89**: 677–83.
8. Cawley JC, Burns GF, Hayhoe FGJ. *Hairy Cell Leukemia*. Berlin: Springer Verlag, 1980.
9. Golde DW. Therapy of hairy-cell leukemia. *N Eng J Med* 1982; **307**: 495–6.
10. Mintz U, Golomb HM. Splenectomy as initial therapy in twenty-six patients with leukemic reticuloendotheliosis (hairy cell leukemia). *Cancer Res* 1979; **39**: 2366–70.
11. Golomb HM, Vardiman JW. Response to splenectomy in 65 patients with hairy cell leukemia: an evaluation of spleen weight and bone marrow involvement. *Blood* 1983; **61**: 349–52.
12. Golomb HM. Progress report on chlorambucil therapy in post-splenectomy patients with progressive hairy cell leukemia. *Blood* 1981; **57**: 464–7.
13. Quesada JR, Reuben J, Manning JT, Hersh EM, Gutterman JU. Alpha interferon for induction of remission in hairy-cell leukemia. *N Eng J Med* 1984; **310**: 15–8.
14. Johnston JB, Glazer RI, Pugh L, Israels LG. The treatment of hairy-cell leukaemia with 2′-deoxycoformycin. *Br J Haematol* 1986; **63**: 525–34.
15. Bouroncle BA, Wiseman BK, Doan CA. Leukaemic reticuloendotheliosis. *Blood* 1958; **13**: 609–30.
16. Neiman RS, Sullivan AL, Jaffe R. Malignant lymphoma simulating leukemic reticuloendotheliosis: a clinicopathologic study of ten cases. *Cancer* 1978; **43**: 329–42.
17. Jacobs P, King HS, Dent DM, Hayes M. Unusual response of lymphocytic lymphoma (not hairy cell leukemia) to splenectomy without chemotherapy. *S Afr Med J* 1984; **65**: 687–9.
18. Narang S, Wolf BC, Neiman RS. Malignant lymphomas presenting with prominent splenomegaly. *Cancer* 1985; **55**: 1948–57.
19. Eldar S, Kemeny MM, Benfield JR. Splenectomy for the treatment of hairy-cell leukemia. *Surg Gynecol Obstet* 1982; **155**: 829–32.
20. Jansen J, Hermans J. Splenectomy in hairy cell leukemia: a retrospective multicenter analysis. *Cancer* 1981; **47**: 2066–76.
21. Myers TJ, Ikeda Y, Schwartz S, Pharmakidis AB, Baldini MG. Primary splenic hairy cell leukemia—remission for 21 years following splenectomy. *Am J Hematol* 1981; **11**: 299–303.
22. Ingoldby CJH, Ackroyd N, Catovsky D, Spencer J. Splenectomy for hairy cell leukaemia. *Clin Oncol* 1981; **7**: 325–31.
23. Ratain MJ, Golomb HM, Vardiman JW, Vokes EE, Jacobs RH, Daly N. Treatment of hairy cell leukemia with recombinant alpha$_2$ interferon. *Blood* 1985; **65**: 644–8.
24. Van Norman AS, Nargorney DM, Martin JK, Phyliky RL, Ilstrup DM. Splenectomy for hairy cell leukemia: a clinical review of 63 patients. *Cancer* 1986; **57**: 644–8.
25. Cawley JC, Worman CP. Hairy cell leukaemia. *Br J Haematol* 1985; **60**: 213–18.

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Skin discoloration following inguinal hernia repair

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Wound infection rates of 0·5–11 per cent have been reported[1–2] following inguinal hernia repair. Wound bruising and haematoma are seldom reported accurately but are generally believed to predispose to wound sepsis and may lead to longer hospital stay or antibiotic prescription. Having noticed a diffuse red discoloration of some wounds, which were not obviously infected, we studied this phenomenon in relation to bruising and infection: we have described it as a 'flare'.

Patients and methods

We studied 351 consecutive inguinal hernia wounds in a 3-year period. Hernia repairs were performed using monofilament nylon darn. The subcutaneous layer was approximated with catgut. Skin closure was not standardized and either polyglycolic acid or polypropylene sutures were used. No patient was given prophylactic antibiotics or subcutaneous heparin. Wounds were inspected daily in hospital and weekly for a month postoperatively. A flare was defined as a diffuse red discoloration of the skin surrounding the wound. This blanched on digital pressure and became yellow before fading. Bruising was defined as blue discoloration of the skin and infection as discharge of pus from the wound.

Results

The categorization of wounds and morbidity are set out in *Table 1*. Only 32 per cent of wounds appeared normal, the remainder having a bruise or flare. There were 16 wound infections (4·6 per cent). Five of these were minor, with extrusion of catgut sutures. No difference was noted in the incidence of flare, bruising and infection between the varying grades of surgeon (*Table 1*). Similarly, there was no significant difference in the depth of subcutaneous fat between those patients having normal, bruised and flared wounds.

Hospital stay was not prolonged for patients with bruised or flared wounds but patients with infected wounds remained in hospital longer. The incidence of infection by wound group is shown in *Table 2* and, although numbers were small, there was no significant difference in the rate of infection between normal wounds and those with a flare or bruise (Fisher's exact test). Of the 16 wound infections, 10 became apparent after discharge from hospital.

Table 2 *Infection related to wound type*

Wound	*n*	Infections	Percentage
Normal	114	2	1·8
Flare	108	8	7·4
Bruise	129	5	3·9
Haematoma	15	1	6·7

Table 1 *Percentage wound morbidity by grade of surgeon*

Wound	Patients (*n*)	Consultant	Senior Registrar	Registrar	SHO	All
Normal	114	30·5	30·8	37·6	30·8	32·5
Flare	108	33·6	30·8	23·7	35·4	30·8
Bruise	129	35·9	38·4	38·7	33·8	36·7
Seroma	34	10·2	6·2	10·8	10·8	9·7
Infection	16	7·0	1·5	2·2	6·2	4·6
Haematoma	15	3·1	4·6	4·3	6·2	4·3

Discussion

This study reflects surgical practice in a district general hospital where hernia repairs are carried out by all grades of surgeon.

The nature of the flare is uncertain but it may be a form of bruising as all flares became yellow before fading. The mechanism may involve initial skin capillary dilatation. A highly conjectural mode of action might be paralysis of the local autonomic control of the arteriolar sphincters by extravasated blood in the subcutaneous tissue space. Neither bruising nor flare have delayed hospital discharge, in contrast to wound infection. Thus, just as pyrexia need not delay patients' discharge[3], neither should a wound with a flare or bruise. A diffuse redness of the wound may be taken to indicate the presence of infection[4], but, although a flare occurred in 1/3 of patients in this report, only 7·4 per cent of these developed sepsis. There is a temptation to treat a flare with antibiotics but, as it is a common phenomenon, this should be resisted in the absence of other signs of sepsis.

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References

1. Cruse PJE. Incidence of wound infection on the surgical services. *Surg Clin N Am* 1975; **55**: 1269–75.
2. Parkash S, Mayooranathan TS, Ananthakrishnan N. Inguinal hernias: a preliminary study on a technique of repair based on the keel principle. *Aust NZ J Surg* 1983; **53**: 3–6.
3. Belham GJ, Emery RJ, Cheslyn-Curtis S, Ralphs DNL. Early discharge despite postoperative pyrexia after inguinal herniorrhaphy in unselected patients. *Br J Surg* 1985; **72**: 973–5.
4. Soul JO, Dewar EP. Bilateral inguinal herniae—a reappraisal of dogma. *J R Naval Med Service* 1984; **70**: 160–2.

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Diseases of the pre-auricular lymph nodes mimicking parotid tumours

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A number of different conditions may present as swellings determined clinically to be within the anatomical boundaries of the parotid gland. Most are parotid tumours but inflammatory conditions of the parotid parenchyma may also present in this way. In a small proportion of patients, the parotid gland is normal and the pathology lies with the pre-auricular lymph nodes. These nodes lie on the surface of the parotid gland and within its substance but superficial to the facial nerve[1–3]. When enlarged, they may mimic parotid tumours. We present 20 patients with diseases affecting these nodes and discuss the diagnosis and management.

Patients and methods

Details of the age, sex and diagnosis of the 20 patients are given in *Table 1*. In 14 patients, the nature of the disease was suspected clinically and proven by aspiration cytology, Tru-cut biopsy or serology. A diagnosis of benign parotid tumour was made in the remaining six cases, who underwent exploration with a view to superficial parotidectomy. During this 4 year period a total of 79 parotidectomies were performed so that the incidence of unexpected pre-auricular node disease was 7·6 per cent.

Ten patients had secondary tumours. In eight cases the nodes contained metastatic malignant melanoma. The primary sites were temple, forehead, scalp, cheek and uvea invading the eyelid. In two patients, the primary tumour and nodal metastasis occurred synchronously while in the remaining six a history of previous excision of a primary malignant melanoma was obtained. Two patients were found to have pulmonary metastases and were treated by chemotherapy. The other six patients were managed by superficial parotidectomy and radical neck dissection. One elderly man with a hard parotid mass and complete ipsilateral facial palsy was found to have a malignant sweat gland tumour of the scalp. The final patient in this group presented with a discrete tumour in the parotid 3 years after a squamous cell carcinoma had been removed from his pinna.

Superficial parotidectomy for suspected benign parotid tumour was performed in four patients with low grade follicular lymphomas and one with toxoplasmosis. The only abnormality on clinical examination in these five patients was a swelling in the parotid region. Another patient with a similar clinical presentation and a normal chest X-ray was also explored with a view to a superficial parotidectomy. During development of the cervical component of the incision, an unsuspected enlarged jugulodigastric node was found and frozen section histopathology suggested tuberculosis which was later confirmed by culture. The parotidectomy was, therefore, abandoned. The pre-auricular swelling disappeared following antituberculous treatment.

Discussion

The correct diagnosis of a swelling arising within the pre-auricular nodes can often, but not always, be suspected from a careful history and thorough clinical examination. Specific factors in the history are previous treatment of a primary tumour in the head and neck, and systemic symptoms in some cases of lymphoma, toxoplasmosis and tuberculosis. Physical examination should include a careful inspection of all primary sites which drain lymph to the pre-auricular nodes and a search for other lymphadenopathy. Chest X-ray should be routine.

Aspiration cytology was used to confirm the clinical diagnosis of metastatic malignancy. Tru-cut needle biopsy is useful for large tumours extending beyond the limits of the parotid gland, and considered initially to be surgically unresectable; this technique provided diagnostic material in the two aggressive lymphomas who presented in this way.

Metastatic carcinoma from primary sites in the head and neck was the commonest cause of enlarged pre-auricular nodes, confirming the findings of Conley and Arena[4]. Metastases from

Table 1 *Diagnosis of 20 patients with enlarged pre-auricular nodes*

Diagnosis	*n*	Sex	Age (years)	Diagnostic investigations
Secondary tumours	10			
Malignant melanoma		F	53	Fine needle aspiration
		F	58	Fine needle aspiration
		F	60	Fine needle aspiration
		M	24	Fine needle aspiration
		M	25	Fine needle aspiration
		M	40	Fine needle aspiration
		M	45	Fine needle aspiration
		M	55	Fine needle aspiration
Squamous cell carcinoma		M	74	Fine needle aspiration
Turban tumour (eccrine cylindroma)		M	76	Biopsy of tumour
Lymphoma	6			
High grade		F	74	Tru-cut needle biopsy
		M	64	Tru-cut needle biopsy
Follicular		F	63	Superficial parotidectomy
		M	30	Superficial parotidectomy
		M	55	Superficial parotidectomy
		M	69	Superficial parotidectomy
Toxoplasmosis	3	F	40	Superficial parotidectomy
		F	32	Serology
		F	34	Serology
Tuberculosis	1	M	28	Exploration, node biopsy

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more distant tumours are rare[5–7] and were not represented in this series.

Lymphoma can affect the pre-auricular nodes either as a solitary focus of disease or as part of an aggressive and disseminated process. Low grade lymphomas can present as a discrete swelling of a node simulating a benign parotid tumour. High grade lymphomas present as rapidly growing, overtly malignant lesions, and a feature is the relative infrequency of facial nerve palsy in contrast to parotid carcinomas and sarcomas[8].

Toxoplasmosis is an important and often unsuspected cause of nodal enlargement. The diagnosis may be suggested by the relatively young age of the patient, a history of keeping cats, other lymphadenopathy, and the presence in some cases of low grade fever, malaise and transient splenomegaly. IgM antibodies can be detected as soon as 5 days after infection and disappear within 6 months. Most patients do not require specific treatment and can be observed until the lymphadenopathy subsides[9,10].

Tuberculosis in the parotid region is rare. It may present with a facial palsy that resolves on antituberculous therapy. The source of infection is uncertain but patients often have no evidence of pulmonary infection[11,12].

In conclusion, a thorough history and clinical examination followed by simple investigations and selective use of needle biopsy allowed a diagnosis to be made in two-thirds of our cases of pre-auricular lymphadenopathy. The remaining patients were thought to have benign parotid tumours and were explored with a view to superficial parotidectomy. A systematic approach to diagnosis minimizes the number of unnecessary parotidectomies.

References

1. Feind CR. *The Lymphatics in Cancer*. Philadelphia: WB Saunders, 1972: 63–6.
2. Marks NJ. The anatomy of the lymph nodes of the parotid gland. *Clin Otolaryngol* 1984; **9**: 271–5.
3. McKean ME, Lee K, McGregor IA. The distribution of lymph nodes in and around the parotid gland: an anatomical study. *Br J Plast Surg* 1985; **38**: 1–5.
4. Conley J, Arena S. Parotid gland as a focus of metastasis. *Arch Surg* 1963; **87**: 757–64.
5. Kucan JO, Frank DH, Robson MC. Tumours metastatic to the parotid gland. *Br J Plast Surg* 1981; **34**: 299–301.
6. Yarrington Ct. Metastatic malignant disease to the parotid gland. *Laryngoscope* 1981; **91**: 517–19.
7. Nichols RD, Pinnock LA, Szymanowski RT. Metastases to parotid nodes. *Laryngoscope* 1980; **90**: 1324–7.
8. Watkin G, MacLennon KA, Hobsley M. Lymphomas presenting as lumps in the parotid region. *Br J Surg* 1984; **71**: 701–2.
9. McLeod R, Remington JS. In Petersdorf RG *et al*. eds. *Harrison's Principles of Internal Medicine* 10th ed, New York: McGraw-Hill, 1983: 1200–5.
10. Moran WJ, Tom DWK, King GD, Silverman ML. Toxoplasmosis lymphadenitis occurring in a parotid gland. *Otolaryngol Head Neck Surg* 1986; **94**: 237–40.
11. Kant R, Sahi RP, Mahendra NN, Agarwal PK, Shankhdhar R. Primary tuberculosis of the parotid gland. *J Indian Med Assoc* 1977; **68**: 212.
12. Yaniv E, Avedillo M. Parotid tumour as a presenting symptom of tuberculosis. *S Afr Med J* 1985; **68**: 613.

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Technique of testicular fixation for torsion of the testis

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Testicular torsion is a surgical emergency which requires prompt intervention. The affected side should be explored to confirm the diagnosis. The testis must then be untwisted, examined for its viability, and bilateral testicular fixation should be performed, unless the affected side has infarcted in which case it should be removed.

A variety of techniques for testicular fixation have been described, involving placing sutures through the tunica albuginea to the lower pole[1], lateral wall[2] or median septum of the scrotum[3]. We describe a simple and effective method of fixing the testis to the median scrotal septum.

Technique

A single transverse scrotal incision is made through skin and dartos, giving easy access to both testes (*Figure 1*). The tissue plane between the tunica vaginalis and the median septum on the affected side is opened by blunt dissection. The testis is then delivered and the tunica vaginalis incised. After confirming the diagnosis, the testis is untwisted and its viability confirmed. Two Allis's forceps are introduced to grasp the upper and lower ends of the median septum (*Figure 2*) which is then everted outside the wound. Three interrupted 3/0 silk or Vicryl (Ethicon Ltd, UK) sutures are placed through the tunica albuginea and the median septum (*Figure 3*). After returning the testis to its hemiscrotum, the procedure is repeated on the other side.

Discussion

The simple step of grasping the upper and lower ends of the median septum to evert it outside the wound is the secret that makes this an easy and swift procedure. The choice of the suture material to anchor the testis remains with the surgeon.

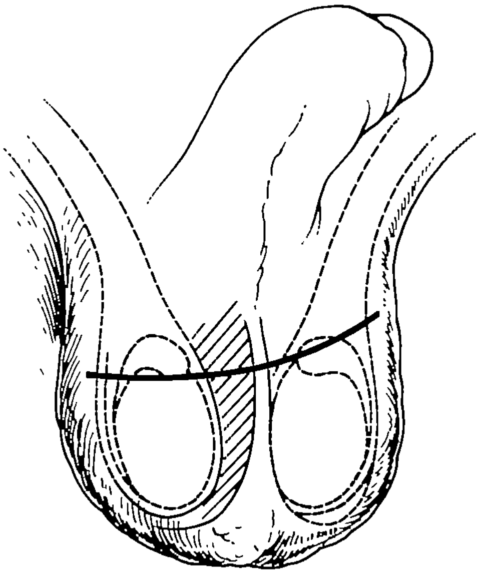

Figure 1 *Transverse incision for exploring both sides of the scrotum*

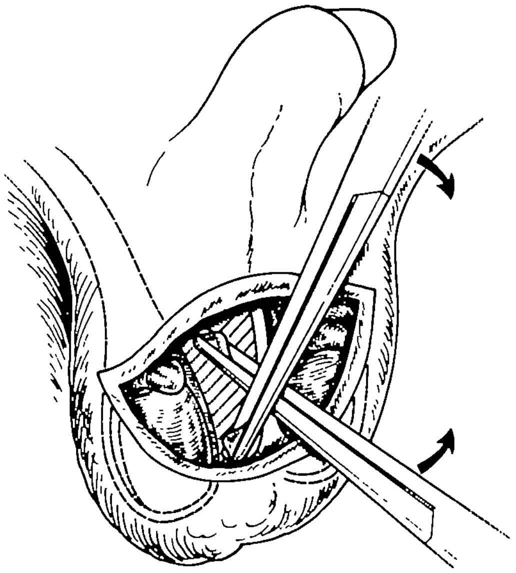

Figure 2 *Allis's forceps grasping upper and lower ends of median septum*

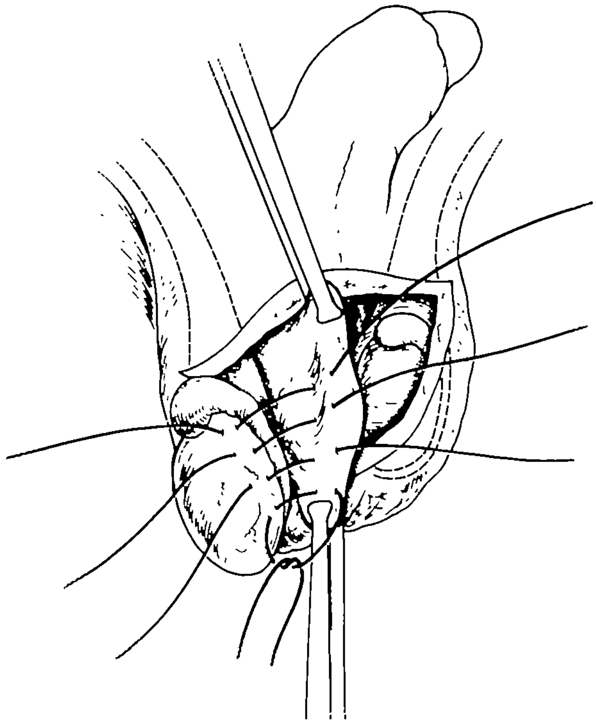

Figure 3 *Sutures fixing the tunica albuginea to the median scrotal septum*

Acknowledgements

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References

1. Dudley HAF, ed. In: *Rob and Smith Atlas of General Surgery*, First ed. London: Butterworths, 1983: 538–40.
2. Rintoul RF. In: *Farqharson's Textbook of Operative Surgery*, Sixth ed. Edinburgh: Churchill Livingstone, 1978: 929–30.
3. Eckstein HB, Hohenfellner R, Williams DI. In: *Surgical Paediatric Urology*, London, Stuttgart: Saunders, Thieme, 1977: 462.

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Coarctation of the suprarenal aorta: a new surgical approach

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Coarctations of the abdominal aorta involving its inter- and suprarenal segment are usually operated on through a thoraco-abdominal approach. We describe a modified access of the lower part of the descending aorta through the diaphragm. It was successfully used for the treatment of two aortic coarctations 5 and 6 years ago.

Surgical technique

A midline incision is made from the xiphoid to the pubis. A subcostal retractor is used to expose the left lateral ligament of the liver, which is divided. The liver is retracted towards the right, the lesser omentum is incised longitudinally.

The access to the thoracic aorta depends upon the anatomy of the diaphragmatic aortic hiatus and this is variable. In 80 per cent of 60 dissections, the aortic hiatus was found to be formed by two layers, one superficial and one deep, and with two variations.

In the most frequent variation (65 per cent) the superficial layer is formed only by the direct fibres of the right crus, which should not be divided but only dissected free from the oesophagus and retracted towards the right after the division of the arcuate ligament, if present.

In the less frequent variation (15 per cent) the superficial layer is reinforced by a crossing fibrous band, arising from the left crus; this layer must be divided. The deep layer, which is always present, is formed by a thick fibrous band arising from the right crus. It is adherent to the aorta, which it crosses and then becomes the left border of the oesophageal hiatus (*Figure 1*). This band must be divided to approach the aorta.

In the remaining 20 per cent the deep layer does not exist. The aorta is only covered by a superficial crossing band arising from the right crus and the arcuate ligament.

When the two (or only one) layers are divided, and when the pleural reflections are dissected free and retracted, a length of an average of 63 mm of aorta is clearly exposed. The aorta can be cross clamped or interrupted by an intraluminal balloon catheter which allows a longer aortotomy. An end-to-side aorto–aortic graft is inserted from the thoracic aorta to the distal abdominal aorta. The renal arteries can be re-attached directly into the graft or bypassed from the aortic graft, from the aorta below the graft or from an iliac artery. Synthetic materials should be avoided in children and young adults.

This technique was used for the treatment of a coarctation of the abdominal aorta in two boys with hypertension, who were 14 and 15 years old. Both renal arteries and the mesenteric artery were stenotic in the two cases. A bypass was inserted between the supracoeliac aorta and the aorta below the coarctation. In both cases the left renal artery was re-implanted into the aortic graft and the right renal artery was revascularized by a 6 mm polytetrafluoroethylene (PTFE) graft. In one of the patients the superior mesenteric artery was grafted from the aortic prosthesis by an 8 mm PTFE graft. Both patients were asymptomatic 5 and 6 years later and the angiograms showed the good patency of the grafts (*Figure 2*).

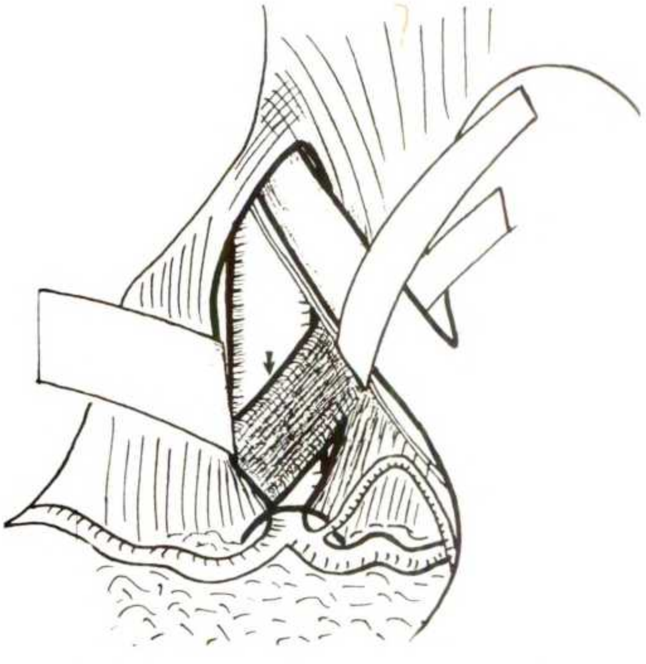

Figure 1 *Diagram of the aortic hiatus showing the deep layer of the right crus (arrow) which must be divided to approach the supracoeliac aorta*

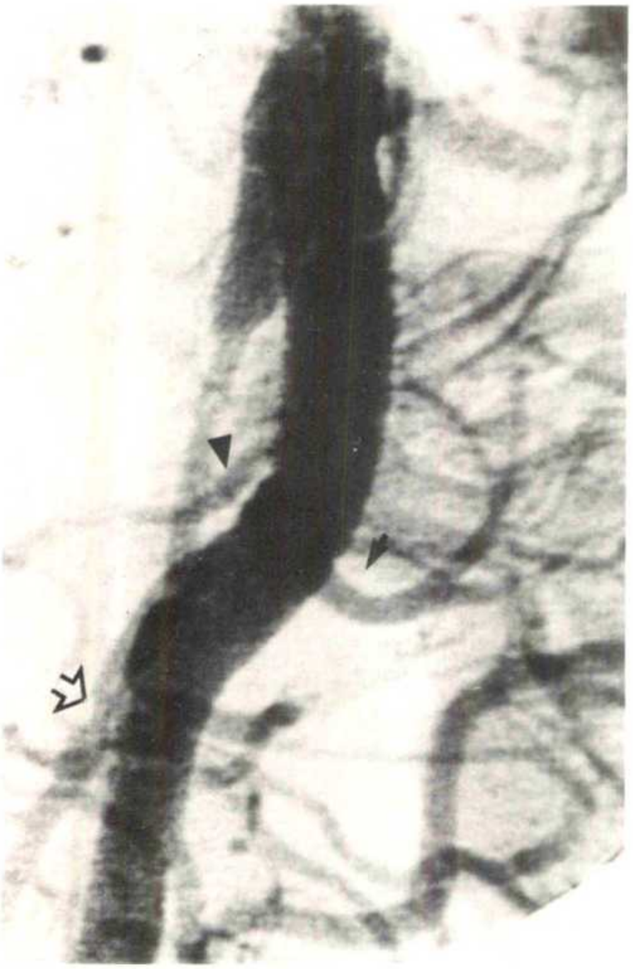

Figure 2 *Aortogram of case 1, 6 years after aorto-aortic bypass operation. Revascularization of the right renal artery (arrow head), the left renal artery (arrow) and the superior mesenteric artery (open arrow)*

Discussion

The origin of these lesions is controversial[1–6], but their surgical treatment has been standard using a left thoraco-abdominal

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approach, even in the more recent series[7,8]. The single abdominal approach is easier to perform than the thoracic and abdominal one. It leaves the thorax free for a possible future access. It allows one-stage treatment of the lesions of the aorta and its branches.

The specific complications of this access are rare: the opening of the pleura can be neglected or briefly drained. Cardio-oesophageal reflux may be theoretically induced by the division of the right crus of the diaphragm. A fundoplication may prevent this, but no reflux was observed in these two patients without that prevention.

When the treatment of an inter- or suprarenal coarctation of the aorta is indicated, the implantation of a prosthesis on the descending aorta through a single abdominal approach is an easy and effective option.

References

1. De Bakey ME, Garrett HE, Howell JP, Morris GC. Coarctation of the abdominal aorta with renal arterial stenosis: surgical considerations. *Ann Surg* 1967; **165**: 830–43.
2. Graham LM, Zelenock GB, Erlandson EE, Coron AG, Lindenauer SM, Stanley JC. Abdominal aortic coarctation and segmental hypoplasia. *Surgery* 1979; **86**: 519–24.
3. Hallett JW, Brewster DC, Darling RC, O'Hara PJ. Coarctation of the abdominal aorta. Current options in surgical management. *Ann Surg* 1980; **191**: 430–7.
4. Scott HW, Dean RH, Boerth R, Sawyers JL, Meacham P, Fischer RD. Coarctation of the abdominal aorta. Pathophysiologic and therapeutic considerations. *Ann Surg* 1979; **189**: 746–57.
5. Thevenet A, Mary H, Boennec M, Benhamou A. Coarctations et dysplasie de l'aorte abdominale. A propos de 9 observations. *Ann Chir Thorac Cardio Vasc* 1978; **17**: 187–96.
6. Vaysse J, Nussaume O, Kieffer E, Lacombe M, Andreassian B. Les coarctations et hypoplasies de l'aorte abdominale. Revue générale à propos de 21 observations personnelles. *J Chir* 1978; **115**: 71–87.
7. Vaccaro PS, Myers JC, Smead WL. Surgical correction of abdominal aortic coarctation and hypertension. *J Vasc Surg* 1986; **3**: 643–8.
8. Messina LM, Goldstone J, Ferrell LD, Reilly LM, Ehrenfeld WK, Stoney RJ. Middle aortic syndrome. Effectiveness and durability of complex arterial revascularization techniques. *Ann Surg* 1986; **204**: 331–9.

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Cavo-atrial shunt with externally stented PTFE graft for Budd–Chiari syndrome with caval obstruction

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The clinicopathological feature of Budd–Chiari syndrome is so complicated that a sophisticated approach is necessary. Side-to-side portacaval shunt[1] or mesocaval shunt[2] may be useful if the inferior vena cava is patent, and meso-atrial shunt[2] or similar operations[3] may be indicated if the inferior vena cava is obstructed.

Case report

A 33-year-old man was admitted with ascites and oesophageal varices. Inferior cavography showed obstruction of the inferior vena cava just above the patent right hepatic vein. The left and middle hepatic veins were not visualized (*Figure 1a*). Endoscopic examination demonstrated prominent oesophageal varices. Coeliac arteriography showed a patent portal vein. It was thought that a cavo-atrial shunt would be effective in relieving the congestion of both the portal vein and the inferior vena cava because the right hepatic vein was patent below the caval occlusion. Laparotomy was performed through a right subcostal incision. A moderate amount of serous ascites was found. The liver was fibrous and markedly engorged. The initial pressures of the portal vein and inferior vena cava were 410 and 360 mmH$_2$O, respectively. Right thoracotomy was undertaken by cutting the right costal arch in the seventh intercostal space (*Figure 2*). Side-to-side anastomosis was first made between the inferior vena cava just above the right renal vein and an expanded polytetrafluoroethylene (PTFE) graft. A hole was made by blunt dissection at the posteromedial portion of the right diaphragm; the graft was passed behind the liver and then anastomosed to the right atrium (*Figure 2*). Post-shunt portal and inferior caval pressures were 295 and 195 mmH$_2$O, respectively. No complications were encountered during surgery. The postoperative course was uneventful. Ascites disappeared completely after operation. Liver function and hypersplenism were significantly improved by the shunt. Cavography taken 21 days postoperatively showed the graft to be patent throughout its length (*Figure 1b*). One month after the operation, the oesophageal varices had nearly disappeared. Patency of the shunt was confirmed 15 months later. The patient has been living a normal life for 21 months after operation without any anticoagulant therapy.

Discussion

In making meso-atrial or cavo-atrial shunts most surgeons have used Dacron (C. R. Bard Inc., Massachusetts, USA) or Teflon (DuPont UK Ltd, Stevenage, UK) grafts. The late patency rate with these materials is not necessarily satisfactory when used in the portal system. In fact, graft thrombosis occurred in three out of seven patients with a Dacron meso-atrial shunt in the series of Cameron *et al.*[2]. Segadal *et al.*[3] have used a PTFE graft in this type of operation. The shunt of their patient is reported to have been

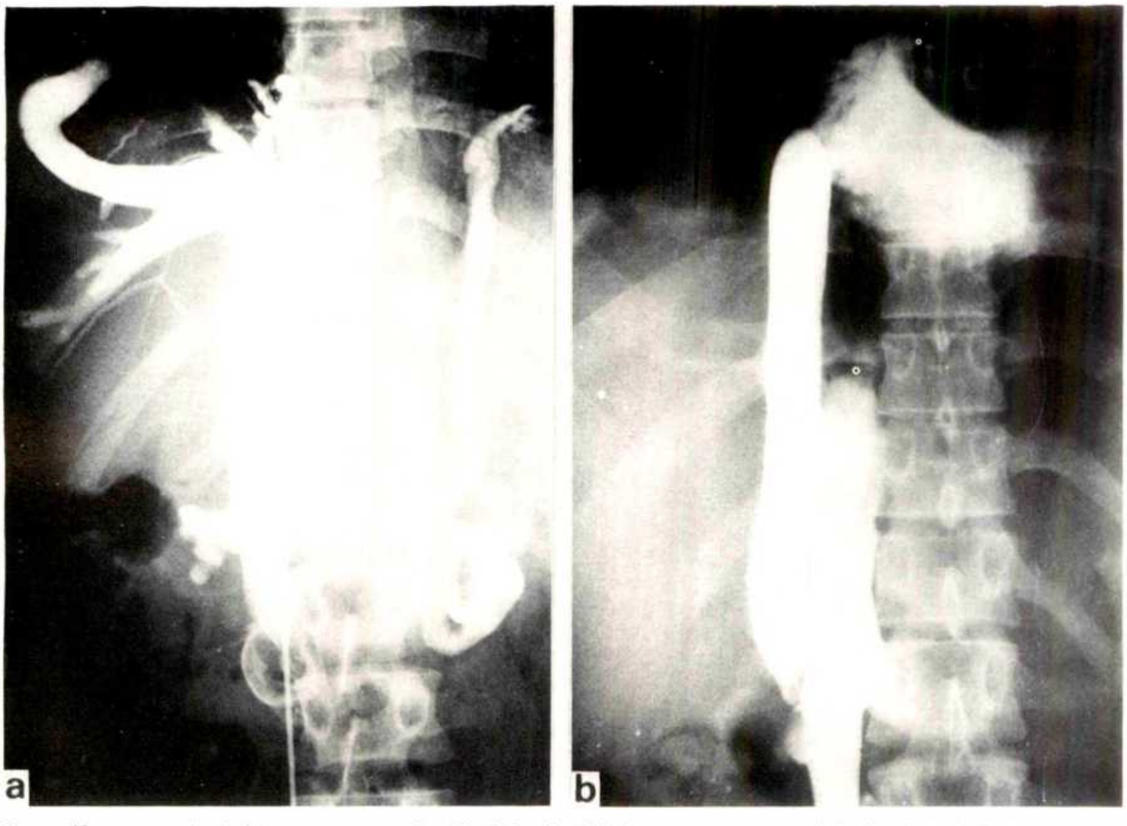

Figure 1 **a** *Pre- and* **b** *postoperative inferior vena cavography. The left and middle hepatic veins were occluded but the right hepatic vein was patent just below the caval obstruction of 1·5 cm long* (**a**). *Patency of the shunt was confirmed 21 days after cavo-atrial shunt* (**b**)

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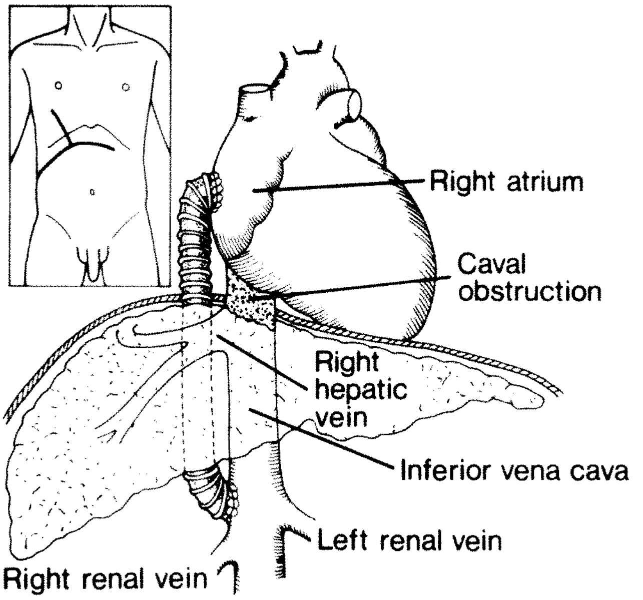

Figure 2 *Operative technique. A PTFE graft with external rings was interposed behind the liver between the suprarenal inferior vena cava and the right atrium*

patent for 3 years but continued anticoagulant therapy was required. Recently, Victor *et al.*[4] reported five patients with constriction of the inferior vena cava on whom dorsal cavo-atrial shunt had been successfully carried out using PTFE grafts. In the last patient they used a ringed PTFE graft as we did in our patient. The late patency of the shunt was confirmed in all their patients 21–38 months after operation. However, they do not indicate whether anticoagulant therapy was used. We have not administered any anticoagulant drugs to our patient and the shunt remains patent at 21 months. We were able to pass the graft through the shortest way behind the liver without kinking or compression because of its supporting external rings. Several groups, including ourselves[5,6], have suggested the advantages of PTFE for portal decompression procedures. We have an excellent late patency rate without anticoagulant therapy in distal splenorenal shunt using PTFE interposition grafts. The current experience may indicate that PTFE with external rings is a promising material for treatment of the Budd–Chiari syndrome with obstruction of the inferior vena cava.

References

1. Orloff MJ, Yohansen KH. Treatment of Budd–Chiari syndrome by side-to-side portacaval shunt: experimental and clinical results *Ann Surg* 1978; **188**: 494–512.
2. Cameron JL, Herlong HF, Sanfey H *et al.* The Budd–Chiari syndrome: treatment by mesenteric-systemic venous shunts. *Ann Surg* 1983; **198**: 335–46.
3. Segadal L, Arnesjo B, Halvorsen JF, Gothlin J, Myking A, Solberg CO. Budd–Chiari syndrome with obstruction of the inferior caval vein: successful treatment by cavosplenoatrial shunt. *Surgery* 1985; **98**: 63–7.
4. Victor S, Jayanthi V, Kandasamy I, Ratnasabapathy A, Madanagopalan N. Retrohepatic cavoatrial bypass for coarctation of the inferior vena cava with a polytetrafluoroethylene graft. *J Thorac Cardiovasc Surg* 1986; **91**: 99–105.
5. Rosenthal D, Deterling RA Jr, O'Donnell TF Jr, Gallow AD. Interposition grafting with expanded polytetrafluoroethylene for portal decompression. *Surg Gynecol Obstet* 1979; **148**: 387–90.
6. Nagasue N, Ogawa Y, Yukaya H, Hirose S. Modified distal splenorenal shunt with expanded polytetrafluoroethylene interposition. *Surgery* 1985; **98**: 870–7.

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Spontaneous iliacocaval arteriovenous fistula: the case for differential diagnosis

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Arteriovenous fistulae which originate at the level of the iliac vessels are rare. Most are acquired through trauma; the incidence is 1·7 per cent out of 539 traumatic arteriovenous fistulae[1]. Spontaneous fistulae of the iliac vessels are mostly related to the presence of an atherosclerotic aneurysm of the common iliac arteries. To date, only 14 cases of spontaneous arteriovenous fistulae of the iliac vessels, involving the common iliac artery and vein, have been reported. The case presented is unique because there was a spontaneous connection between the right common iliac artery and the inferior vena cava.

Case report

A 65-year-old man was seen in the emergency room by the medical team complaining of dyspnoea at rest, abdominal pain and swelling of the left lower limb. The patient had a past history of smoking.

He was moderately distressed and dyspnoeic. There was hypotension and a tachycardia; the respiratory rate was 28/min. A 10 cm pulsatile abdominal mass was palpable low in the midline and right flank, with a prominent thrill, and a rough continuous murmur was audible in the abdomen. There was jugular venous distension, gallop rhythm and liver enlargement. In addition, the clinical feature of a deep venous thrombosis of the left lower limb, with extreme swelling just to the level of the inguinal ligament, was seen. The clinical diagnosis of congestive heart failure, probably due to an abdominal aortic aneurysm which had ruptured into the inferior vena cava, was made. A CT scan was performed, and the diagnosis of abdominal infrarenal aortic aneurysm was confirmed.

At surgery, no blood was found in the peritoneal cavity or in the retroperitoneum. A 10 × 10 cm pulsatile mass was seen at the level of the aortic bifurcation. The infrarenal abdominal aorta was of normal calibre (*Figure 1*). Control of the proximal aorta, iliac arteries distal to the mass, inferior vena cava and common iliac veins was difficult and careful dissection was needed to identify all the structures involved. An intense thrill was noted. After a longitudinal incision was made into the mass, a 2 cm communication between the right common iliac artery and the inferior vena cava just proximal to the junction of the iliac veins was found. The venous structures were controlled with Foley catheters.

Thrombectomy of the left common iliac vein was attempted but abandoned, as the Fogarty catheter passed only 10 cm; the iliac venous orifice was oversewn. The longitudinal incision in the fistula was prolonged up to the inferior vena cava and distally to the right common iliac vein, and venous reconstruction was performed using part of the wall of the fistula, which was sutured with a continuous running 4/0 Prolene (Ethicon, UK) suture. Patency of the iliacocaval axis was then completed. Because of the thin and very friable arterial walls, a bifurcated 16 × 8 mm aorto-iliac Dacron (C. R. Bard Inc., Massachusetts, USA) graft was used. A Saratoga (Sherwood Medical Industries, Ireland) sump drain was left in place.

Abdominal re-exploration was performed 48 h later because of continued bleeding through the sump, but no active bleeding point was identified. The postoperative course was complicated by ileus and sepsis, but the patient gradually improved. Congestive heart failure was controlled with digitalis and diuretics. Swelling and oedema of the left lower limb disappeared and the patient was discharged in good condition 51 days after the operation, and is currently doing well 5 months postoperatively.

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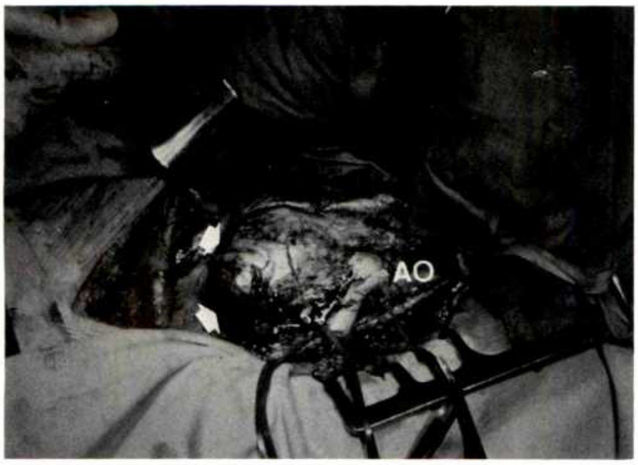

Figure 1 *Operative photograph showing the aortic bifurcation and the aneurysmal arteriovenous fistula involving the right common iliac artery (arrows)*

Discussion

Spontaneous arteriovenous fistulae of the iliac vessels have recently been studied by McAuley *et al.*[2]. Only 15 cases of spontaneous iliac fistulae have been reported and this is the only one with a direct communication between the right common iliac artery and the inferior vena cava[3–15].

The previously reported cases presented with: (1) congestive heart failure due to the elevated cardiac output; (2) pulsatile abdominal mass with a murmur and thrill and (3) acute ischaemia of the lower limbs or signs of deep venous thrombosis. McAuley *et al.*[2] considered that this is a unique and distinct syndrome; however, the diagnosis can be confused with an abdominal aortic aneurysm ruptured into the inferior vena cava[16,17].

Pre-operative differential diagnosis is usually not made by non-invasive methods. Only angiography can help the surgeon to establish the exact diagnosis before the operation. In our case, computerized axial tomography showed a picture of abdominal aortic aneurysm but the use of contrast material would probably have been helpful. However, the diagnosis of iliacocaval fistula was only confirmed at surgery when a normal calibre infrarenal aorta was discovered and a giant pulsatile mass occupying the area of the aortic bifurcation was seen.

Iliacocaval reconstruction was performed using part of the wall of the fistula as autogenous material for venous repair and arterial reconstruction with a bifurcated aorto-iliac graft as previously stated in the literature.

Prompt recognition of this clinical condition and an aggressive surgical treatment are of importance in the successful surgical management of this uncommon condition.

References

1. Heberer G, Rau G, Löhr HN. *Aorta und Grosse Arterien*. New York: Springer-Verlag, 1966.
2. McAuley CE, Peitzmann AB, de Vries EJ, Silver MR, Steed DL, Webster MW. The syndrome of spontaneous iliac arteriovenous fistula. A distinct clinical and pathophysiologic entity. *Surgery* 1986; **99**: 373–7.
3. Zajtchuk R, Yacoub MH, Kittle CF. Spontaneous arteriovenous fistula between the right common iliac vessels. *Surgery* 1971; **69**: 194–200.
4. Reckless JPD, McColl I, Taylor GW. Aorto-caval fistulae: An uncommon complication of abdominal aortic aneurysm. *Br J Surg* 1972; **59**: 461–2.
5. Birnholz JL. Radionuclide angiography in the diagnosis of aortocaval fistula. *J Thorac Cardiovasc Surg* 1973; **65**: 292–5.
6. Kazmier FJ, Harrison GE. Acquired aortocaval fistulas. *Am J Surg* 1973; **55**: 175–83.
7. Auer AI, Sauer DC, Levin M. Iliac arteriovenous fistula from an aneurysm following seat belt trauma. *Angiology* 1974; **25**: 21–3.
8. Datta PK, Vickery CM. Arteriovenous fistula from rupture of major arterial aneurysms. *J R Coll Surg Edinb* 1979; **24**: 165–6.
9. Fourmestraux N, Jault F, Duclos F *et al.* Fistule arterioveineuse iliaque primitive par rupture spontanée d'un anevrysme athéromatheux. *Ann Chir* 1980; **34**: 439–42.
10. Lo G, Galli G, Pampari GC, Spaggiari A, Motta R. Le fistole arteriovenosa acquisite: A proposito di un case din aneurisma dell'arteria iliaca destra fistolizzato nella vena iliaca sinistra. *Acta Biomed Ateneo Parmense* 1981; **52**: 117–23.
11. Willis JS, Herrera L, Kester R. Spontaneous arteriovenous fistula between common iliac artery and vein. *Cardiovas Intervent Radiol* 1982; **5**: 246–8.
12. Du Toit D, Van der Merwe DM, Groenwald JH, de Roubaix JAM. High-output cardiac failure associated with an iliac artery aneurysm and arteriovenous fistula. *S Afr Med J* 1983; **63**: 293–4.
13. Richards DD. Spontaneous fistula between a right common iliac artery aneurysm and iliac vein. *JAMA* 1984; **251**: 1189–90.
14. Duda AM, Mandel DM, Piasio MA. Bilateral isolated iliac artery aneurysm with arteriovenous fistula. *Contemp Surg* 1984; **25**: 27–35.
15. Singer I, Morris JG. Detection of arteriovenous fistula between common and external iliac artery and vein by radionuclide angiography. *Clin Nucl Med* 1984; **9**: 551–3.
16. Landes RG, Trumbull HP, Nicoloff DM. Abdominal aortic aneurysm with rupture into the inferior vena cava associated with horseshoe kidney. *Ann Surg* 1978; **187**: 329.
17. Baker WH, Sharzer LA, Ehrenhaft JL. Aortocaval fistula as a complication of abdominal aortic aneurysm. *Surgery* 1972; **72**: 933–8.

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Lymphangiosarcoma complicating chronic primary lymphoedema

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Malignant change is an uncommon but serious complication of chronic lymphoedema. We report a patient in whom this complication was initially misdiagnosed as cellulitis.

Case report

The patient developed primary lymphoedema of the left leg at the age of 14. There was no family history of limb swelling and lymphangiography showed the presence of hypoplastic lymph vessels, confirming the diagnosis of primary lymphoedema. The patient was treated conservatively with compression stockings and he attended hospital once a year for follow-up.

Twenty-one years later, aged 35 years, he complained of a red and slightly raised area on his left shin, which had been present for a few days. This was thought to represent an area of cellulitis. He was treated with antibiotics, instructed to elevate his leg at home and arrangements were made to admit him for a surgical reduction operation. However, the initial skin lesion increased in size, ulcerated and new areas appeared proximally. Although concerned, the patient deferred seeking medical advice until his next appointment. When seen, most of the lower limb was covered by raised, red-purple lesions and the initial area had become a fungating, foul-smelling ulcer. An urgent incision biopsy confirmed the diagnosis of lymphangiosarcoma and, because of the extent of the involvement, he was treated by cytotoxic chemotherapy and radiotherapy with some initial resolution. The tumour is now extending again and the prognosis is extremely poor.

Discussion

Lymphangiosarcoma was first reported by Stewart and Treves in 1948 as a complication of chronic lymphoedema after mastectomy[1]. Since then, most of the reported patients have developed this complication in long-standing secondary lymphoedema after radical mastectomy (with and without radiotherapy). The condition has also been described in patients with long-standing primary lymphoedema and has become known as the Stewart–Treves syndrome[2,3].

The aetiology of lymphangiosarcoma complicating chronic lymphoedema is not known. As radiation induces many types of angiosarcoma, it may be a contributing factor in some cases, but malignant change can develop without prior irradiation[2]. The clinical features of lymphangiosarcoma are characteristic[2]. The lesion first appears as a solitary, purplish-red, slightly raised area in the skin and may masquerade as a bruise or an area of cellulitis. Similar satellite tumours develop and the lesions grow rapidly.

There is no established treatment for lymphangiosarcoma complicating chronic lymphoedema. Prompt radical amputation of a limb affected by a localized lesion has produced a number of patients who have survived 5 years and may offer the best hope of cure[2,3]. Wide local excision is usually associated with early recurrence and poor survival. For inoperable cases, radiotherapy has been reported to produce useful palliation (and a few long-term survivors) but the results of chemotherapy are generally disappointing[2,3].

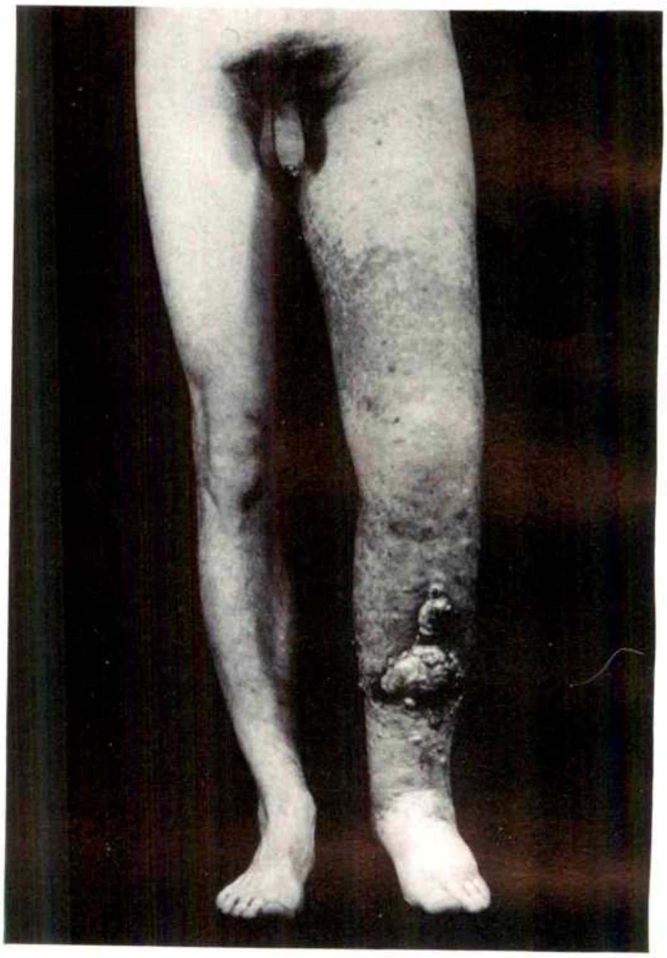

Figure 1 *Lymphangiosarcoma complicating chronic primary lymphoedema, showing nodules and ulceration*

Lymphangiosarcoma is an uncommon complication of long-standing lymphoedema. The overall prognosis is poor: in the largest published series, the median survival was 19 months[2]. However, early diagnosis and radical surgery may improve the prognosis[2]. A patient complaining of 'bruises' or who develops red macules or nodules in an area of chronic lymphoedema should undergo urgent biopsy. Cellulitis should be diagnosed with caution and suspicion heightened if there is not a prompt improvement with treatment. It has been suggested that careful follow-up will lead to early diagnosis[4]. However, the tumour is rapidly growing and may develop between hospital visits. Patients should be specifically instructed to report early to hospital if 'bruises' or areas of 'cellulitis' develop in their lymphoedematous limb.

References

1. Steward FW, Treves N. Lymphangiosarcoma in postmastectomy lymphoedema: a report of six cases in elephantiasis chirurgica. *Cancer* 1948; **1**: 64–81.
2. Woodward AH, Ivins JC, Soule EH. Lymphangiosarcoma arising in chronic lymphoedematous extremeties. *Cancer* 1972; **2**: 562–72.
3. Sordillo PP, Chapman R, Hajdu SI, Magill GB, Golbey RB. Lymphangiosarcoma. *Cancer* 1981; **7**: 1674–9.
4. Lymphangiosarcoma in chronic lymphoedema: reports of 3 cases and review of the literature. *Acta Chir Scand* 1986; **152**: 227–30.

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Suture granuloma simulating a cholangiocarcinoma

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Benign biliary strictures not caused by surgical trauma are rare. We present the case of a man who presented with jaundice 17 years after having a cholecystectomy. This was due to compression of the biliary tree by a suture granuloma.

This is the first such case reported in the world literature.

Case report

A 68-year-old man presented in August 1985, with a 10 day history of dark urine, pale faeces and jaundice. Previous surgery included a cholecystectomy for gallstones in 1968.

Physical examination confirmed the jaundice but otherwise was non-contributory and liver function tests confirmed the clinical impression of obstructive jaundice.

Ultrasound showed dilated intraheptic ducts but could not identify the common bile duct. A percutaneous transhepatic cholangiogram performed through the right lobe of the liver showed a dilated intrahepatic duct system with no flow of contrast down the common bile duct. A presumptive diagnosis of cholangiocarcinoma was made. At laparotomy, following difficult dissection of adhesions, a 2 × 3 cm mass was found in the porta hepatis and a peroperative cholangiogram (*Figure 1*) showed a constriction in the region of the bifurcation of the common hepatic duct. Prolonged dissection of the mass separated it from the common hepatic duct which it had been compressing and revealed a silk suture in the core of the mass. Histology of the mass showed the wall of the cystic duct with surrounding florid fibrosis and foreign body giant cells, the majority of which contained refractile suture material. There was no evidence of carcinoma.

The patient made an uneventful postoperative recovery. Six weeks later, a T-tube cholangiogram was performed which showed no obstruction to contrast flow in the common hepatic duct. The T-tube was removed and when last reviewed in the out-patients department, 8 months postoperatively, the patient was well and his liver function tests had returned to normal.

Discussion

It is well known that obstructive jaundice can be produced by obstruction, constriction or compression of the extrahepatic biliary tree[1]. Although most benign strictures of the biliary tree are caused by surgical trauma, stenosis of the bifurcation of the common hepatic duct is usually caused by primary carcinoma arising in the wall of the duct or by neoplastic invasion of the hilar lymph nodes[2]. Localized segments of sclerosing cholangitis in this region have also been reported.

The presence of ultrasonographically determined dilated intrahepatic ducts with a common bile duct of normal size is suggestive of proximal bile duct blockage. In such a case, percutaneous transhepatic cholangiography can localize the exact site and the nature of the obstruction[3]. Although this is the investigation of choice, it does on occasion incorrectly diagnose neoplastic lesions[3,4]. Even at the time of surgery, the benign nature of the lesion may not be certain but this may be confirmed histologically if the lesion is fully resected[4].

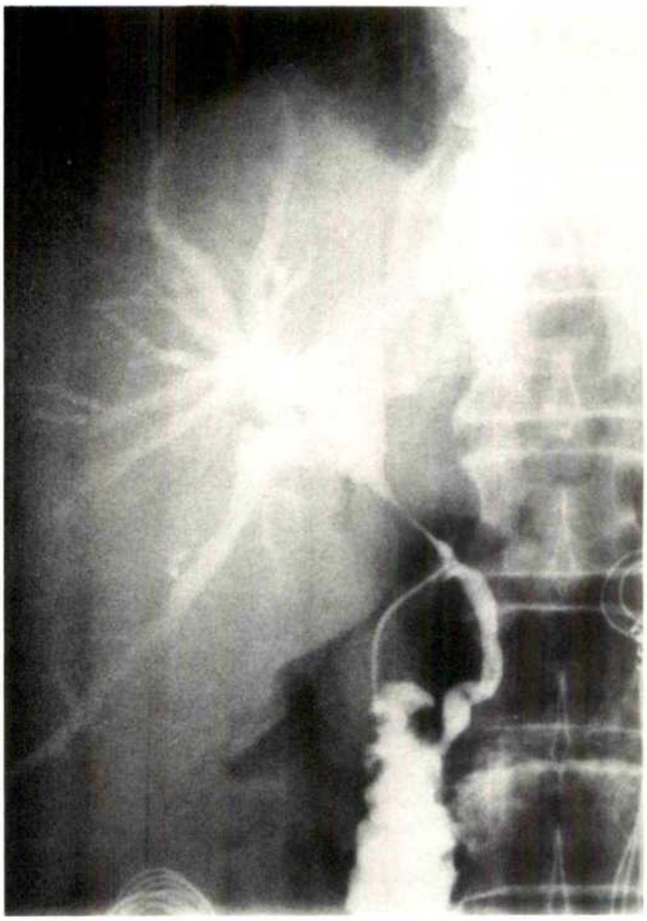

Figure 1 *Peroperative cholangiogram demonstrating the common hepatic duct stricture*

Much has been written with regard to the complications which may arise from the various suture materials used in biliary surgery. Homan in 1897 described the first case of a silk suture used in cholecystectomy giving rise to the subsequent formation of common bile duct stones[5]. Up until 1983, there were 71 cases in which operative residues gave rise to the need for surgery[6]. In most cases, silk was the offender but stones have also been formed around linen, nylon, Dacron (C. R. Bard Inc., Massachusetts, USA) and chromic catgut.

Although suture granulomas have simulated neoplasms in the stomach and the bladder, we believe this is the first reported case to do so in the biliary system.

References

1. Barnett SM, Davidson ED. Obstructive jaundice secondary to non-biliary extrahepatic inflammatory disease. *Am Surg* 1979; **45**: 618–20.
2. Sherlock S. *Diseases of the Liver and Biliary System*. Oxford: Blackwell, 1975.
3. Smadja C, Bowley NB, Benjamin IS *et al*. Idiopathic localized bile duct structures: relationship to primary sclerosing cholangitis. *Am J Surg* 1983; **146:** 404–8.
4. Hadjis NS, Collier NA, Blumgart LH. Malignant masquerade at the hilium of the liver. *Br J Surg* 1985; **72:** 659–61.
5. Homan J. Gallstones formed around silk sutures, twenty months after recovery from cholecystectomy. *Ann Surg* 1897; **26:** 114–16.
6. Garcia JC, Lemarcha DF, Samama G. Corps étrangers des voies biliaires. *Sem Hop Paris*, 1983; **59:** 120–8.

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Idiopathic segmental infarction of the greater omentum

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Idiopathic segmental infarction of the greater omentum is an uncommon cause of acute abdominal pain mimicking appendicitis or cholecystitis. Before laparotomy the diagnosis is hardly ever considered. Just over 150 cases have been reported since this phenomenon was first described by Bush in 1896[1].

Case reports

Case 1

A 30-year-old man, previously in perfect health, was seen with a few days history of increasing abdominal pain; the pain had started in the right lower quadrant but migrated to the right subcostal region. There was no nausea or vomiting. On physical examination there was direct and rebound tenderness over the right side of the abdomen. Bowel sounds, body temperature, white blood cell count (WBC) and urinalysis were normal. Ultrasonography of the gallbladder revealed no abnormalities. With a pre-operative diagnosis of appendicitis the patient was operated upon. The abdomen was opened by a gridiron incision (McBurney) and some free serosanguineous fluid aspirated. The appendix was normal but, nevertheless, removed. On further exploration a mass was palpated in the greater omentum near the hepatic flexure of the colon. As this mass could not be exposed, a second incision was made in the right subcostal region. An infarcted segment of the greater omentum was found adhering to the ascending colon. There was no sign of torsion or herniation; the gallbladder, duodenum and colon were normal. After limited resection of the infarcted segment the patient made an uneventful recovery and was discharged on the sixth day.

Histological examination revealed extensive vascular congestion, proliferation of connecting tissue and non-specific inflammation.

The patient was re-admitted 3 weeks later with a 3-day history of high fever, chills and anorexia, later accompanied by pain in the right subcostal region and right shoulder. He looked ill and was extremely tender in the right upper abdominal quadrant. His temperature was 38·6°C and the WBC had risen to 12·4 × 10^9 cells/l. On exploration, the omentum at the previous excision site was thickened and firmly adherent to the ascending colon as if a bowel perforation had been sealed off. No perforation was found and the abdomen was closed. Antibiotic treatment was started although later blood cultures were negative.

Postoperative colonoscopy revealed no abnormalities in the transverse and ascending colon. The patient made a quick recovery and is in good health 1 year later.

Case 2

A 46-year-old man was seen with a history of a few days abdominal pain in the right lower quadrant. There was nausea but no vomiting.

On examination there were signs of localized peritoneal irritation slightly above McBurney's point. His temperature was 37°C, erythrocyte sedimentation rate (ESR) 2 mm/h, and the WBC was 10·9 × 10^9 cells/l. The diagnosis of acute appendicitis was made and a laparotomy performed. The appendix appeared normal but a small (5 × 5 cm) infarcted segment of the greater omentum was found adhering to the ascending colon. The segment was excised, and the appendix was also removed. The postoperative course was uneventful and the patient was discharged 5 days later. On microscopic examination the same histological changes were seen as in the first case.

Two days after discharge, the patient was re-admitted with abdominal pain of sudden onset and fever (38·4°C). He had localized tenderness just above the scar, an ESR of 35 mm and the WBC was 10·9 × 10^9 cells/l. Given our experience with the previous patient, conservative treatment seemed justified. After nasogastric suction and parenteral feeding he made a rapid recovery, was discharged after 1 week and has remained in good health.

Discussion

Idiopathic segmental infarction of the greater omentum should be distinguished clearly from the more common condition of torsion of the greater omentum. In idiopathic segmental infarction no other intra-abdominal pathological condition is present. The infarction is primary, limited to a small segment, and not due to such conditions as portal venous thrombosis, congestive heart failure and strangulation. Infarction may occur at all ages, even in young children; the presumption that obesity predisposes to this disease has not been confirmed[2]. The male: female ratio is 2:1.

Aetiology is not clear and several speculative theories have been postulated. The high incidence of involvement of the right side of the omentum, adherent to the ascending colon, caecum or anterior peritoneum, is best explained by a developmental abnormality. In the embryo the dorsal mesogastrium develops into the greater omentum, the ventral mesogastrium into the lesser omentum; occasionally an abnormal extension of the ventral mesogastrium develops and later becomes united with the greater omentum. This additional part may become adherent to the ascending colon and even to the caecum or anterior peritoneum (Haller's ligament). Its blood supply is delicate and liable to infarction.

Venous engorgement after heavy meals is another suggested aetiological factor together with increased intra-abdominal pressure (coughing, laughing) and the gravitational pull on the greater omentum in obese persons. The thin-walled veins are stretched, resulting in thrombosis and extravasation. Also, an infectious cause has been suggested but not proven[3].

The symptoms of infarction are non-specific; patients present with abdominal pain of a few days duration usually in the right side of the abdomen. Nausea, vomiting and diarrhoea may be present but, like in appendicitis, are not very common. The physical findings are variable but, typically, maximum tenderness is slightly higher than McBurney's point though lower than that normally found in acute cholecystitis. Temperature is normal or slightly raised, while the WBC may be elevated. It is not surprising that omental infarction is often misdiagnosed as appendicitis or cholecystitis.

The finding of free sero-sanguineous fluid at laparotomy must raise suspicion. The, usually, well-demarcated infarcted area of the omentum should always be excised to prevent adhesion formation and the risk of secondary sepsis[4]. Appendicectomy may be safely performed at the same time.

Why both our patients re-developed the abdominal symptoms, after an apparently uneventful postoperative course, is not fully understood. We have not found any similar cases in other reports. A possible explanation might be continued or repeated infarction of the omentum. Since only a limited resection of the macroscopic infarcted part was performed, the blood supply of the adjacent area might have been compromised at that time. This could imply that wide excision is advisable.

References

1. Bush P. A case of haemorrhage into the greater omentum. *Lancet* 1896; **i**: 286.
2. Epstein LI, Lempke RE. Primary idiopathic segmental infarction of the greater omentum: case report and collective review of the literature. *Ann Surg* 1968; **167**: 437–43.
3. Crofoot DD. Spontaneous segmental infarction of the greater omentum. *Am J Surg* 1980; **139**: 262–4.
4. Patchell RD. A fatal case of idiopathic omental infarction. *West Virginia Med J* 1977; **73**: 29–30.

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Insulinoma and ganglioneuroma

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Insulinoma is a rare tumour with an annual incidence in the order of one per million[1,2]. The incidence of isolated ganglioneuroma is not known. Pancreatic islet cell tumours may be a solitary abnormality, but they are a well recognized part of the MEN Type I syndrome[3–5] when they are usually multiple both in site and in the number of hormones produced. Mucosal and alimentary-tract ganglioneuroma have been reported as part of the MEN Type IIb syndrome[6,7]. While the familial nature of these conditions has been reported[8–10], the sporadic occurrence of multiple tumours in one individual requires consideration[11,12]. This is a particular problem with regard to MEN Type IIb as, although it is considered to be an autosomal dominant condition, due to its rarity, the degree of gene penetrance and range of expression are not known[13]. In addition, this syndrome is associated with shortened survival and, therefore, reduced reproductive capability.[13]

We report the finding of an insulinoma and adrenal medullary ganglioneuroma in a young woman with no family history of endocrine disease.

Case report

A 26-year-old woman with no family history of endrocrine disease presented with an 8 month history of grand mal seizures which investigation showed to be hypoglycaemic in origin.

The diagnosis of insulinoma was confirmed by fasting blood glucose concentrations of 1·2 mmol/l and 1·0 mmol/l with simultaneous serum insulin concentrations of 32·4 and 32·8 milliunits/l, respectively. Full blood count, serum calcium, prolactin and cortisol were normal, as were chest X-ray and skull X-ray. Fasting plasma concentrations of glucagon, pancreatic polypeptide, gastrin, VIP (vasoactive intestinal polypeptide) and neurotensin were all normal, and urinary metadrenalines less than 1·0 μmol/24 h. Coeliac axis angiography failed to localize a tumour.

Abdominal CT scan showed a large mass indenting the upper medial pole of the left kidney, containing some areas of calcification. During laparotomy a large solid retroperitoneal tumour 10 cm in diameter was found lying behind the pancreas and extending from the front of the left kidney to the hilum of the spleen. After removal of this mass, a well encapsulated pancreatic tumour 1·5 cm in diameter was identified just distal to the neck of the pancreas, and a partial pancreatectomy was performed.

Histology of the pancreatic tumour confirmed it to be an insulinoma and immunohistochemistry showed the presence of immunologically reactive insulin within the cytoplasm of the cells. Negative reactions were obtained when staining for glucagon, somatostatin and pancreatic polypeptide. Histology of the retroperitoneal tumour revealed this to be a ganglioneuroma which appeared to have arisen within the adrenal medulla.

Discussion

The report of three unrelated families with familial phaeochromocytoma and islet cell tumour of the pancreas[14], and other case reports of tumour combinations belonging to both MEN Type I and MEN Type II[15], suggest that the three MEN syndromes may not be totally distinct entities, but that overlapping syndromes may exist. The large international survey by Stefanini *et al.*[16] found that of 951 cases of insulinoma with complete pathological findings 4 per cent were associated with an additional neoplasm. Our patient showed none of the physical features associated with MEN Type IIb and this condition has only been associated with multiple mucosal and alimentary tract ganglioneuromatosis. There has been one previous case report of the association between insulinoma and ganglioneuroma, both arising in the pancreas, in a 15 year old boy[17]. While this and our case may simply illustrate the coincidence of two rare tumours, the possibility of a true association should be considered, particularly in view of the suggested embryological derivation of all these tumours from neural crest tissue[18]. This unifying theory for the origin of all multiple endocrine neoplasia is, however, not universally accepted.[12,19]

References

1. Kavlie H, White TT. Pancreatic islet beta cell tumors and hyperplasia: Experience in 14 Seattle hospitals. *Ann Surg* 1972; **175:** 326–35.
2. Frerichs H, Creutzfeldt W. Hypoglycaemia. I. Insulin secreting tumours. *Clin Endocrinol Metab* 1976; **5:** 747–67.
3. Underdahl LO, Woolner LB, Black BM. Multiple endocrine adenomas; report of 8 cases in which the parathyroids pituitary and pancreatic islets were involved. *J Clin Endocrinol Metab* 1953; **13:** 20–47.
4. Wermer P. Genetic aspects of adenomatosis of endocrine glands. *Am J Med* 1954; **16:** 363–71.
5. Moldawer M, Nardi GL, Raker JW. Concommitance of multiple adenomas of the parathyroids and pancreatic islets with tumour of the pituitary. A syndrome with familial incidence. *Am J Med Sci* 1954; **228:** 190–206.
6. Block MB, Roberts JP, Kadair RG, Seyfer AE, Hull SF, Nofeldt FD. Multiple endocrine adenomatosis Type IIb. *JAMA* 1975; **234:** 710–14.
7. Carney JA, Go VLW, Sizemore GW, Hayles AB. Alimentary-tract ganglioneuromatosis. A major component of the syndrome of multiple endocrine neoplasia, Type 2b. *N Engl J Med* 1976; **295:** 1287–91.
8. Johnson GJ, Summerskill WHJ, Anderson VE, Keating FR. Clinical and genetic investigation of a large kindred with multiple endocrine adenomatosis. *N Engl J Med* 1967; **277**: 1379–85.
9. Snyder N, Scurry MT, Deiss WP. Five families with multiple endocrine adenomatosis. *Ann Intern Med* 1972; **76:** 53–8.
10. Schimke RN. Genetic aspects of multiple endocrine neoplasm. *Ann Rev Med* 1984; **35:** 25–31.
11. Andersson A, Bergdahl L. Insulinomas and multiple endocrine neoplasia. *Acta Chir Scand* 1976; **142:** 297–300.
12. Marks V. Pancreatic hypoglycaemia — other causes. In: Marks V, Rose FC, eds. *Hypoglycaemia*. Oxford: Blackwell, 1981: 158–78.
13. Schimke RN. Syndromes with multiple endocrine gland involvement. *Progr Med Genet (NS)* 1979; **3:** 143–75.
14. Carney JA, Go VLW, Gordon H, Northcutt RC, Pearse AGE, Sheps SG. Familial pheochromocytoma and islet cell tumor of the pancreas. *Am J Med* 1980; **68:** 515–21.
15. Hansen OP, Hansen M, Hansen HH, Rose B. Multiple endocrine adenomatosis of mixed type. *Acta Med Scand* 1976; **200:** 327–31.
16. Stefanini P, Carboni M, Patrassi N, Basoli A. Beta-islet cell tumors of the pancreas: Results of a study on 1067 cases. *Surgery* 1974; **75:** 597–609.
17. Bodner E, Lederer B, Margreiter D. Ganglioneurom und Insulinom im Pankreas. *Chirurg* 1972; **43:** 420–2.
18. Pearse AGE, Polak JM. Neural crest origin of the endocrine polypeptide (APUD) cells of the gastrointestinal tract and pancreas. *Gut* 1971; **12:** 783–8.
19. Stevens RE, Moore GE. Inadequacy of APUD concept in explaining production of peptide hormones by tumours. *Lancet* 1983; **i:** 118–19.

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Functioning vagal body tumour

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Paragangliomas occurring in the vagus nerve in the neck are rare. In 1983 Tannir *et al.* gleaned 75 cases from the literature[1]. Since then there have been reports of eight other cases. One definite[1] and one probable[2] functioning vagal paraganglioma (VBP) have been reported.

Case report

A 41-year-old woman was seen with a tumour on the right side of the neck which had been present for 6 years, and had slowly enlarged. She complained of discomfort in the area and pain in the throat, bouts of violent coughing and sometimes vomiting after any pressure on the tumour, and palpitations.

She was tall, very thin and had multiple small pigmented naevi on most parts of her body. Blood pressure fluctuated up to 190/120 mmHg and pulse rate was 80/min. A 6 × 4 cm, hard, mobile, non-pulsatile tumour was found behind the angle of the right mandible. Pressure elicited violent coughing and bradycardia. No bruit was heard over the tumour, there were no enlarged lymph nodes in the neck and full ENT examination was negative.

The tumour was thought to be a vagal paraganglioma because of the reflex coughing and vomiting. Digital subtraction angiography showed a tumour blush in the region of the internal carotid artery just above the bifurcation but without splaying of the carotid arteries. CT scan showed a solid tumour which could not be separated from the carotid vessels (*Figure 1*). The base of the skull was intact. The 24-hour urinary nor- and metanephrine excretion was 14·5 μmol (normal 0–5), 3-methoxy-4-OH-mandelic acid excretion was 87·7 μmol (normal 7·5–36) and vanilmandelic acid excretion was 86 μmol (normal 7–36). MIBG scan showed focally increased activity on the right side of the neck, suggesting that the tumour was the source of excess catecholamine production.

The patient's blood pressure was stabilized during a 14-day preparation with phenoxybenzamine. On exploration, a vascular tumour was found between the internal carotid artery and the jugular vein, partially surrounding the artery anteriorly. The vagus nerve passed through the tumour. The tumour was easily separated from the carotid artery and excised with the involved segment of vagus nerve.

Catecholamine levels 2 weeks postoperatively were normal. The patient was hoarse postoperatively but by 2 months this had disappeared. The right vocal cord was paralysed but the left cord compensated well. Mild hypertension was easily controlled by α-methyldopa.

The tumour measured 5 × 3 × 2·5 cm and was well encapsulated. Microscopically, it was found to have a rich vascular supply with cells arranged in strings and cell nests. There were small argyrophyllic granules in the cytoplasm. Electron microscopy revealed membrane-bound, electron-dense cytoplasmic granules.

Discussion

Vagal paragangliomas (VPs) arise from the superior or inferior vagal ganglion[3]. The superior (jugular) ganglion lies in the jugular foramen and tumours of this structure grow along the base of the skull or have a dumb-bell component in the posterior cranial fossa. The inferior (nodose) ganglion lies below the base of the skull where the accessory nerve fibres join the vagus nerve. This ganglion contains cell bodies of the afferent fibres of the vagus nerve. Tumours of the inferior ganglion present behind the angle of the jaw. They lie between the jugular vein and the internal carotid artery, displace the artery medially, and do not produce the splaying of the carotid bifurcation seen with carotid body tumours[1].

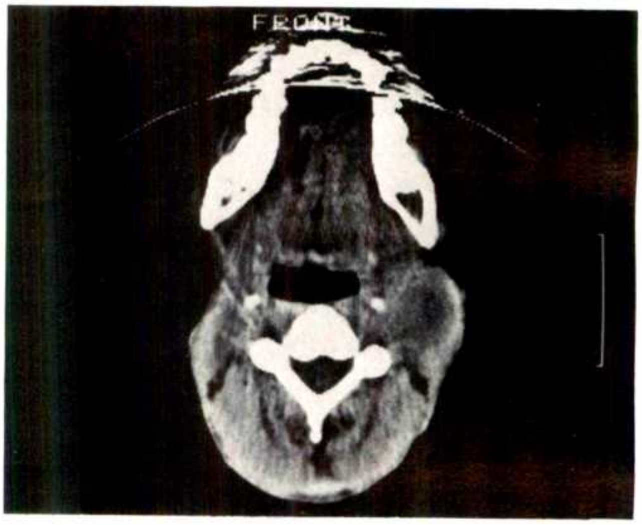

Figure 1 *CT scan demonstrating the tumour behind the angle of the mandible on the right. Scale bar, 5 cm*

Catecholamine production by paragangliomas is now well-documented and is most often seen with retroperitoneal tumours but also occurs with glomus jugulare and carotid body tumours. All paragangliomas are capable of producing a phaeochromocytoma-like syndrome but the present case is only the third reported case of this occurring in a VP.

Tannir *et al.*[1] reported the first definite case of a functioning VP, the tumour secreting noradrenaline. Their patient was grossly hypertensive and was cured by resection of the tumour. Levit *et al.*[2] described a functioning paraganglioma arising from the jugular bulb but which could well have been a VP. The propensity to secrete catecholamines is probably related to the neuro-ectodermal origin of the paraganglia. This concept is further strengthened by the description of tumours producing serotinin[4] and calcitonin[5]. Both adrenaline and noradrenaline have been found in paragangliomas although they mainly secrete noradrenaline[1,5]. The enzyme for conversion to adrenaline, namely *N*-methyl transferase, is usually only present in the adrenal medulla.

The search for a tumour causing a phaeochromocytoma-like syndrome should include all sites of paraganglion tissue. It is also advisable to screen all patients with possible paragangliomas for secretion of catecholamines in view of the hazards of surgery in these patients. Principles of management of patients with functioning paragangliomas should be as for phaeochromocytoma including pre-operative α-adrenergic blockade, specialized anaesthetic management and minimal manipulation of the tumour during surgery.

References

1. Tannir NM, Cortas N, Allam C. A functioning catecholamine-secreting vagal body tumor. *Cancer* 1983; **52**: 932–5.
2. Levit SA, Sheps SG, Espinsoa RE, Harrison EG. Catecholamine-secreting paraganglioma of glomus jugulare region resembling pheochromocytoma. *N Engl J Med* 1969; **281**: 805–11.
3. Glenner GG, Grimley PM. Tumors of the extra-adrenal paraganglion system (including chemoreceptors). In: *Atlas of Tumor Pathology, Series 2, Fascicle 9*. Washington DC: Armed Forces Institute of Pathology, 1974.
4. Farrior JB, Hyams VJ, Berke RH, Farrior JB. Carcinoid apudoma arising in a glomus jugulare tumor: Review of the endocrine activity in glomus jugulare tumors. *Laryngoscope* 1980; **90**: 110–19.
5. White MC, Hickson BR. Multiple paragangliomata secreting catecholamines and calcitonin with intermittent hypercalcaemia. *J R Soc Med* 1979; **72**: 532–8.

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Anterior sacral meningocoele: magnetic resonance imaging and surgical management

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Anterior sacral meningocoele is a rare presacral tumour. Diagnosis can be difficult and there is a lack of agreement regarding the best approach to surgical treatment[1]. We report a case in whom magnetic resonance imaging (MRI) diagnosed and localized the lesion without the need for myelography. The surgical approach to this condition is discussed.

Case report

A 64-year-old Caucasian man was admitted with left-sided lower abdominal swelling. The patient had had intermittent swelling of the legs for several years and admitted to some difficulty with micturition. He had found that he could improve his urinary flow by manual suprapubic pressure. Examination confirmed a cystic mass arising from the pelvis. There were no other abnormal physical signs and in particular no neurological abnormalities in the lower limbs. Plain X-rays of his pelvis showed a bony defect in the sacrum and coccyx and an ultrasound examination and intravenous pyelogram showed a cystic mass in the pelvis compressing the bladder. The diagnosis of an anterior sacral meningocoele was confirmed by MRI (*Figure 1*). As the patient had symptoms of bladder dysfunction it was considered wise to attempt surgical decompression. To ascertain the relationship of the sacral nerves to the meningocoele a posterior approach was selected. A sacral laminectomy was performed and the lower end of the theca identified. This appeared dilated and thin and upon opening it the mouth of the meningocoele could be seen anteriorly. The root of S_2 on the left took an unusual course on the wall of the sac, passing downwards before looping up to enter the root sheath. On the right side the neural anatomy was normal. However, ligation of the neck of the sac distorted several sacral nerve roots and so the defect could only be narrowed with a suture and then closed with an intradural fascial graft.

Initial postoperative recovery was uneventful, but during the following week the meningocoele refilled and this was confirmed by ultrasound scans. An anterior approach was selected for re-exploration and through a midline incision the retrorectal space was opened to expose the large (10 × 11 × 15 cm) meningocoele. The neck of the sac was displayed and ligated with nylon. The front of the bony defect was reinforced with a sheet of polyvinyl sponge. The abdomen was closed without drainage. Postoperative recovery was complicated by retention of urine and transurethral prostatectomy was performed. Further recovery was uncomplicated. An MRI scan before discharge confirmed that the meningocoele had been eliminated. Three months later his only complaint was of numbness around the perineum. Examination confirmed slight diminution of sensation to pinprick on the buttocks, but no other neurological abnormalities.

His two-year-old granddaughter has since been found to have an anterior sacral meningocoele.

Discussion

The surgical approaches to presacral meningocoele include the posterior trans-sacral by laminectomy, the perineal, and the anterior transabdominal approach. The posterior operation allows identification and preservation of the nerve roots, but watertight closure of the pedicle may not be possible. The anterior operation needs experience with the exposure but in our patient was otherwise straightforward; with the pedicle previously identified and cleared of nerve roots it allowed radical amputation of the meningocoele. Although the abdominal operation offers easier closure of the neck of the sac the nerve roots cannot be protected using this approach alone.

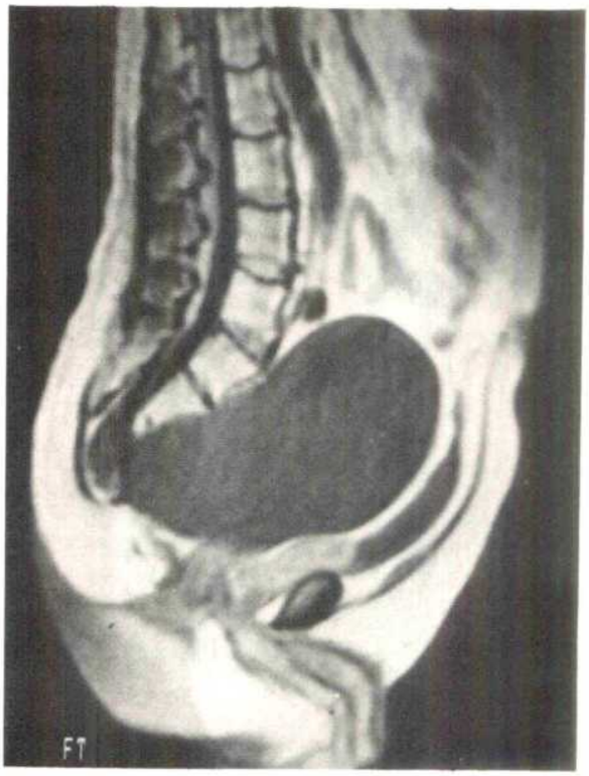

Figure 1 *Sagittal magnetic resonance imaging scan (SE1000/40) showing a large pelvic cyst in continuity with the sacral canal*

Relatively few cases of anterior sacral meningocoele have been reported[2–5] and our computer search shows no previous reports of MRI scanning in this condition. The majority (122 cases) were reviewed by Wilkins and Odom[5] who found that it was more common in females (3:1) and that the majority presented before the age of 30 years. A positive family history was obtained in only two of the cases in their review. Simple aspiration of the cyst was ineffective and carried a very high incidence of meningitis, as did operation via the perineum. Among the cases where operative details were known the lesion was approached via the abdomen or by laminectomy in approximately equal numbers. Laminectomy yield a 'cure' without significant complication in 24 out of 28 cases compared with 12 out of 25 for the abdominal approach. The majority of the bad results were due to meningitis (3 known cases, 1 fatal, after laminectomy; 9 known cases, 4 fatal, after abdominal surgery). Only one of the deaths attributed to meningitis occurred in the pre-antibiotic era. The mortality after laminectomy was <4 per cent but was 24 per cent after abdominal surgery alone. There were two recurrences after laminectomy and three after the abdominal operation alone (9 per cent). Three patients underwent both approaches, each because the first operation had failed; the abdominal operation preceded laminectomy in two of these and all three cases ultimately had satisfactory outcomes.

In our opinion a combined anterior and posterior approach permits both the protection of nerve roots and the radical extirpation of the sac. MRI distinguishes a meningocoele from other presacral tumours and obviates the previously unavoidable need for myelography.

References

1. Uhlig BE, Johnstone RL. Presacral tumours and cysts in adults. *Dis Colon Rectum* 1975; **18**: 581–96.
2. Jackman RJ, LeMon Clark P, Smith ND. Retrorectal tumours. *J Am Med Assoc*. 1951; **145**: 956–62.
3. McColl I. The classification of presacral cysts and tumours. *Proc R Soc Med* 1963; **56**: 797–8.
4. Stewart RJ, Humphreys WG, Parks TG. The presentation and management of presacral tumours. *Br J Surg* 1986; **73**: 153–5.
5. Wilkins RH, Odom GL. Anterior and lateral spinal meningocoeles. In: Vinken PJ, Bruyn GW, eds. *Handbook of Clinical Neurology, Volume 32*. Amsterdam: Elsevier North-Holland Biomedical Press 1978; 193–230.

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Small bowel obstruction caused by bezoars from intestinal diverticuli

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The first serious study of gastrointestinal bezoars was made by the Persian physician Mahamud Bin Masud in the sixteenth century. The first human bezoar, a trichobezoar, was described in 1779 by Baudamant but it was 1883 before Schonborn first removed one through a gastrostomy.

Bezoars are usually formed in the stomach and may migrate into the small intestine, impacting in the terminal ileum causing intestinal obstruction. Two cases are reported of bezoars forming in intestinal diverticuli, and subsequently presenting with acute small bowel obstruction in one case and a mixed picture of perforation and obstruction in the other.

Case reports

Case 1

A 65-year-old lady was admitted as an emergency complaining of anorexia, vomiting, colicky abdominal pain and constipation. A barium meal was performed which showed a large, empty, diverticulum in the second part of the duodenum and dilated small bowel, but no cause for mechanical small bowel obstruction. Twelve days after admission a laparotomy was performed and a bezoar found obstructing the mid-ileum. The bezoar was removed through an enterotomy and she made an uneventful recovery. Section of the bezoar revealed it was composed of vegetable material with a tomato skin at its centre. When last seen, 6 months after surgery, she was well and asymptomatic.

Case 2

A 64-year-old man presented as an emergency with a history of 2 h severe epigastric pain and vomiting. He had a 5-year history of postprandial epigastric pain and fullness which had been extensively investigated with two barium meals and an abdominal ultrasound; the only abnormalities were a small hiatus hernia and a radio-opaque density in the left upper quadrant. Abdominal examination showed him to have diffuse peritonitis. Plain abdominal films showed multiple dilated loops of small bowel with fluid levels and a radio-opaque density overlying the sacrum. An erect chest X-ray showed free gas under the left hemidiaphragm.

At laparotomy a bezoar was found obstructing the mid-ileum with five small areas of necrosis in the immediately proximal small bowel. There were also a number of diverticuli in the upper jejunum. The bezoar was milked back into the proximal small bowel and removed with 10 cm of jejunum containing the largest 2·5 cm wide diverticulum. The small necrotic patches in the ileum were oversewn. It was found that the bezoar fitted within the diverticulum and was able to pass through the mouth of it with relative ease. Subsequent review of the patient's past barium meals showed the bezoar lying within the jejunal diverticulum in the left upper quadrant (*Figure 1*) was the same opacity seen overlying the sacrum on his acute admission.

He made an uneventful postoperative recovery. He was seen in out-patients 3 months later and had no further symptoms of postprandial epigastric pain and fullness.

Discussion

Diagnosis of an intestinal bezoar is not always easy, as Debakey and Ochsner[1] pointed out in their classic description, with most cases presenting variable symptoms of anorexia, vomiting and central abdominal pain. In neither of the cases reported was the diagnosis made pre-operatively. In the first case there was a 2-week delay before surgery but in the second case, although surgery was ultimately undertaken as an emergency because of intestinal obstruction and perforation, symptoms due to the bezoar had been present for over 5 years and these disappeared after his operation.

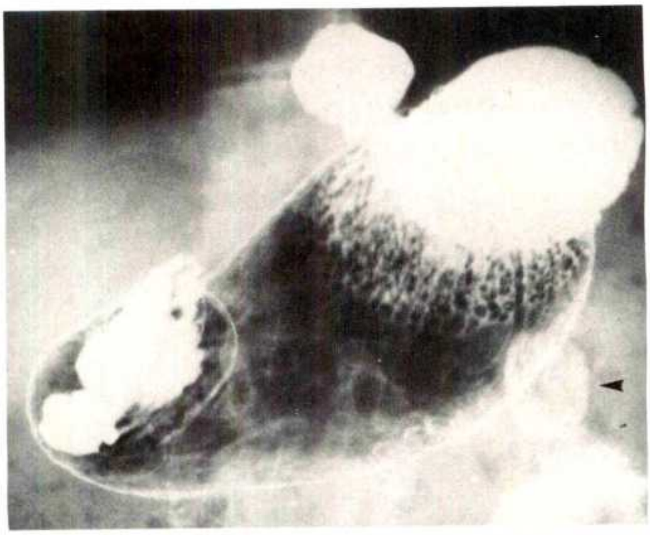

Figure 1 *Review of a previous barium meal from the second patient showed the bezoar lying in a jejunal diverticulum (arrowed) and this subsequently migrated into the distal small bowel causing obstruction and perforation*

Bezoars are usually formed in the stomach, most frequently after gastroduodenal surgery, and then migrate into the small bowel causing intestinal obstruction. In a recent Israeli series of persimmon seed bezoars, 77 consecutive patients over a 5-month period had all undergone previous ulcer surgery[2]. Bezoars have also been recorded as occurring in both the oesophagus[3] and colon[4]. Shocket and Simon recently reviewed the world literature and found eight bezoars originating from duodenal diverticuli, eleven from jejunal diverticuli and three from patients with diverticuli in both the duodenum and jejunum[5]. One further case of intestinal obstruction from a bezoar originating from a duodenal diverticulum has recently been recorded[6].

Intestinal diverticuli are relatively common. In a post-mortem series, duodenal diverticuli were found in 2·8 per cent and jejunal or ileal diverticuli in 4·6 per cent of 218 consecutive examinations[7]. Wheeler found duodenal diverticuli in 7·1 per cent of 2000 consecutive barium meals[8]. However, bezoar formation in one of these intestinal diverticuli and subsequent migration into the lumen of the gut remains a rare cause of intestinal obstruction.

References

1. Debakey M, Ochsner A. Bezoars and concretions; a comprehensive review of the literature with an analysis of 303 collected cases and a presentation of 8 additional cases. *Surgery* 1938; **4**: 934–40.
2. Moriel E, Ayalon A, Eid A, Rachmilewitz D, Krause M, Durst A. An unusually high incidence of gastrointestinal obstruction by persimmon bezoars in Israeli patients after ulcer surgery. *Gastroenterology* 1983; **84**; 752–5.
3. Ford PM, Turner MJ. Intrathoracic bezoar visible on chest radiograph. *Br J Radiol* 1984; 57: 929–32.
4. Farooq P, Nostrant TI, Fiddian-Green RG. 'Giant colonic bezoar' a medication induced bezoar due to psyllium seed husks. *Am J Gastroenterol* 1984; **79**: 319–20.
5. Shocket E, Simon SA. Small bowel obstruction due to enterolith (bezoar) formed in a duodenal diverticulum: a case report and review of the literature. *Am J Gastroenterol* 1982; **77**: 621–4.
6. Mercier V, Lemenager B, Samana G. A new complication of duodenal diverticulum: occlusion of the small intestine by a bezoar. *Ann Chir* 1984; **38**: 691–2.
7. Noer T. Non-Meckelian diverticula of the small bowel. *Acta Chir Scand* 1960; **120**: 175–9.
8. Wheeler D. Cited in Shaw JJM. An unusual case of intestinal obstruction. *Br J Surg* 1941; **28**: 328–9.

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Short note

Br. J. Surg. 1987, Vol. 74, December, 1187

Postoperative seroma following mastectomy and axillary dissection

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A seroma is a collection of fluid which can occur beneath the skin flaps after any form of mastectomy or in the axillary dead space after axillary dissection. The aim of this retrospective study was to find out the incidence of postoperative seroma and to see if its frequency is altered by perioperative treatment with tamoxifen or nodal status of the axilla.

Method

We looked at the clinical records of 108 patients who belonged to a randomized controlled clinical trial comparing postoperative treatment with adjuvant tamoxifen 10 mg b.d. started within 24 h of surgery, against a control group. There were 72 patients who underwent modified radical mastectomy; 17 underwent simple mastectomy with axillary sampling; 6 underwent lumpectomy with axillary sampling and 13 underwent lumpectomy with axillary clearance.

Closed suction drains were removed from the axilla and from beneath skin flaps when drainage was minimal. Records of daily drainage were poorly kept and could not be relied upon for comment. All seromas were tense collections of fluid which required aspiration at least once and developed after drains were removed and before radiotherapy commenced.

Results

The incidence of postoperative seroma is high at 30·6 per cent (*Table 1*). Stratification of the results (*Table 2*) shows a statistically significant difference between the incidence of postoperative seroma in tamoxifen treated patients with positive nodes (57·8 per cent) and those with negative nodes (20·6 per cent) ($0·01 < P < 0·02$). Furthermore the difference between the incidence of postoperative seroma in node positive patients treated with tamoxifen (57·8 per cent) and those that were not (20 per cent) approaches statistical significance ($0·05 < P < 0·1$).

Discussion

This study shows that there appears to be an association between tamoxifen treatment, positive nodes in the axilla and postoperative seroma formation. To explain this we would like to propose the following hypothesis: axillary dissection for positive nodes leads to an increased lymphatic and serous discharge into the axillary fossa and tamoxifen inhibits the adherence of skin flaps to the chest wall.

Breast cancer is known to block lymphatic channels by permeation and tumour growth requires an increased blood supply, often by primitive, fragile vessels. Consequently axillary dissection where there are lymph nodes containing secondary tumour spread gives rise to an increased lymphatic and serous discharge into the axillary fossa.

Table 1 *Incidence of postoperative seroma in patients grouped according to tamoxifen treatment and nodal status of the axilla*

Group	No. of patients	Incidence of postoperative seroma	Statistical analysis
Total	108	33 (30·6%)	
Tamoxifen treated	53	18 (34%)	$\chi^2 = 0·2976$
Control	55	15 (27·3%)	$0·5 < P < 0·7$
Node positive	34	14 (41·2%)	$\chi^2 = 1·9580$
Node negative	74	19 (25·7%)	$0·1 < P < 0·3$

Statistical analysis using the corrected χ^2 test

Table 2 *Stratification of the results*

Group	Total	Node positive	Node negative	Statistical analysis
Tamoxifen treated				
Seroma	18	11 (57·8%)	7 (20·6%)	$\chi^2 = 5·9918$
No seroma	35	8	27	$0·01 < P < 0·02$
Control				
Seroma	15	3 (20%)	12 (30%)	$\chi^2 = 0·1614$
No seroma	40	12	28	$0·5 < P < 0·7$
Statistical analysis		$\chi^2 = 3·5282$ $0·05 < P < 0·1$	$\chi^2 = 0·4312$ $0·5 < P < 0·7$	

Statistical analysis using the corrected χ^2 test

The major pharmacological action of tamoxifen is by competition with oestradiol for a cytoplasmic oestrogen receptor which controls DNA transcription in the nucleus of the tumour cell[1,2]. However, only 50 per cent of advanced breast cancers with oestrogen receptors respond to anti-oestrogen therapy, while up to 15 per cent of those which are oestrogen receptor negative may respond[2]. This raises the question whether tamoxifen exerts some of its effect by another pathway. Tamoxifen has been shown to bind to a cytoplasmic protein in tissues with no oestrogen receptors[1]. There is growing evidence that this secondary action of tamoxifen is by inhibition of growth factors[3]. Platelet-derived growth factors have been isolated from a number of tissues including platelets, human tumours and macrophages. In healing wounds platelet-derived growth factors released from macrophages stimulate fibroblast proliferation[4]. Tamoxifen could therefore contribute to seroma formation by delaying adherence of skin flaps to the chest wall through inhibition of the early stages of collagen synthesis.

References

1. Baum M. Prospects for the future in management of carcinoma of the breast. The biological fallout from clinical trials. *Br J Cancer* 1984; **49**: 117–22.
2. Herxheimer A *et al.* Tamoxifen in breast cancer. *Drug and Ther Bull* 1986; **24**: 17.
3. O'Brian CA, Liskamp RM, Soloman DH, Weinstein IB. Inhibition of protein kinase C by tamoxifen. *Cancer Res* 1985; **45**: 2462–5.
4. Ross R, Bowen-Pope DF, Raines EW. Platelet-derived growth factor, its potential roles in wound healing, atherosclerosis, neoplasia and growth and development. *Ciba Found Symp* 1985; **116**: 98–112.

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Correspondence

Publication lag-times in surgical journals

Sir

The choice of journal to which an original paper should be submitted is a matter of importance for surgeons, clinicians and scientists alike. In many cases this choice is easily made on the basis of subject matter, country of origin, or affiliation of the journal with a particular association or research group. For surgeons wishing to publish an article in a non-specialist surgical periodical, however, it may also be the speed with which papers appear in print that ultimately determines the journal of choice.

We appreciate that most authors will be at least vaguely aware of some variation in publication lag-time amongst journals. However, we felt it would be of some considerable interest to provide a clearer insight into the current speed of publication of the most generally available non-specialist surgical journals.

We therefore collected information available from nine monthly publications during the period January–August 1987. In order to obtain data from at least the 6 most recent issues in which 'original articles' were published, and to ensure that a minimum of 50 articles was included, it was necessary in some journals to extend the search back as far as August 1986. Time from acceptance and/or submission was obtained from the dates quoted by the journal, taking information only from papers variously designated 'original articles', 'research papers', 'original communications', etc. and ignoring those articles whose appearance was based on a paper read at a previous association meeting, or whose content was in the form of a 'case report', 'brief communication', 'clinical note', etc. In addition, similar information was collected from one specialist surgical periodical (*J Thor Cardiovasc Surg*) and one specialist medical/surgical journal (*Gut*), as well as from one general medical periodical (*Br Med J*).

Seven of the general surgical journals provided information about date of acceptance or submission, with one (*Acta Chir Scand*) giving both. There were two journals which did not supply information (*Am J Surg* and *Surg Gynecol Obstet*). It is interesting to note that only in the most recent issue of *Ann R Coll Surg Engl* (bi-monthly) has any indication been given about publication lag-time; of the other three bi-monthly periodicals examined, *Can J Surg* did, while *World J Surg* and *J R Coll Surg Edinb* did not, provide appropriate information. The detailed results of the search are illustrated in *Table 1*.

Table 1 *Time to publication from date of acceptance or submission*

	Time to publication (months)			
	From acceptance		From submission	
Journal	Median	Range	Median	Range
Acta Chir Scand	4	2–7	8	4–13
Annals Surg	—	—	6	4–12
Archives Surg	9	4–16	—	—
Aust N Z J Surg	5	3–8		—
Br J Surg	5	2–8	—	
J Surg Res	—	—	16	11–24
Surgery	7	6–9		
Gut	—	—	8	7–10
J Thor Cardiovasc Surg	12	9–15	14	11–17
Br Med J (weekly)	2	1–4	—	

The wide range of publishing times seen in the seven surgical journals speaks for itself, and comment is neither necessary nor appropriate. It is apparent, however, that such a range is not dissimilar to that found in publications in other fields of specialist interest.

In some journals entire issues are exclusively devoted to papers read at previous association meetings. It should also be stressed that differing policies exist among journals regarding referee review, author revision, etc. It is nevertheless of interest that if publication speed itself is paramount, certain periodicals are clearly more appropriate than others for the submission of manuscripts.

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TPN-associated hepatobiliary dysfunction in the young pig

Sir

We read with interest the report by Truskett *et al.* (*Br J Surg* 1987; **74**: 639–42) concerning a model of TPN-associated hepatobiliary dysfunction in the pig. In all animals, sludge in the gallbladder and a decreased bile salt flow was found which, by definition, constitutes a degree of cholestasis. However, no liver enzyme abnormalities and hyperbilirubinaemia were found, as reported during long-term TPN (> 3 weeks). It is therefore questionable if liver enzyme changes are due to a TPN-induced decrease of bile salt flow.

We studied eight patients with high output stomata in the proximal small bowel and a defunctionalized distal bowel and found liver function abnormalities (intrahepatic cholestasis) during long-term postoperative TPN. Re-infusion of proximal stoma secretions, as described recently[1], resulted, despite ongoing TPN, in complete normalization of liver function abnormalities and hyperbilirubinaemia in all patients. Consequently, TPN by itself did not cause the intrahepatic cholestasis in these patients. We suggest that sequelae of defunctionalization of the distal bowel as bacterial overgrowth and/or related endotoxin production and absorption constitutes an important part of the underlying mechanisms. We propose that in addition to a TPN-induced decrease in bile salt flow other factors like endotoxaemia, which also has been shown to diminish bile salt flow[2], are required to develop overt clinical signs of intrahepatic cholestasis. Similar suggestions can be derived from the findings of Capron *et al.*[3] who demonstrated that treatment with metronidazole completely alleviated signs of intrahepatic cholestasis in patients with Crohn's disease receiving long-term TPN.

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1. Gouma DJ, de Bruyn H, Rinsema W, Soeters PB. Pumping device for re-infusion excretions derived from a proximal jejunostomy or high output fistula. *Br J Surg* 1987; **74**: 741–2.
2. Utili R, Abernathy CO, Zimmerman HJ. Cholestatic effects of Escherichia coli endotoxin on the isolated perfused rat liver. *Gastroenterology* 1976; **70**: 248–53.
3. Capron JP, Gineston JL, Herve MA, Braillon A. Metronidazole in prevention of cholestasis associated with total parenteral nutrition. *Lancet* 1983; **i**: 446–7.

Authors' reply

Sir

D. J. Gouma *et al.* suggest that the defunctioning of the distal small bowel is an important underlying mechanism in the production of clinical cholestasis in association with TPN rather than a secondary factor. We find it difficult to accept this proposition since we have studied the effect of intragastric administration of the TPN solution in the same pig model[1]. Abnormalities of biliary secretion were found and these were similar to those reported by us when the solution was given intravenously (*Br J Surg* 1987; **74**: 639–42). We also observed gallbladder sludge in all our treated animals, but we do not believe that this is necessarily produced by the same mechanism that is responsible for the cholestasis.

It is important to note that deranged liver function occurs in this model in the absence of elevated liver enzyme levels in the serum. Therefore, elevated serum enzyme levels may not be a sensitive indicator of early cholestasis. Clinical cholestasis may become manifest not only when there is an additional hepatic insult such as sepsis, endotoxaemia, or bile salt depletion but also when the TPN is prolonged.

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1. Morgan WP, Truskett PG, Rose MA, Ham JM. Is TPN related hepato-biliary dysfunction secondary to deprivation of enteral stimulation? *Gut* 1986; **27**: A1271.

Anorectal temperature sensation: a comparison of normal and incontinent patients

Sir

I am concerned at the suggestion of Miller *et al.* (*Br J Surg* 1987; **74**: 511–15) that reduced temperature awareness has a role in the pathogenesis of faecal incontinence, and that temperature sensation in the anorectum may allow the discrimination between gas, liquid and solid. Their results have merely shown a deficiency of temperature sensation (as defined by their technique) in the anal canal of patients with idiopathic faecal incontinence (IFI) compared to controls. This is in keeping with earlier findings made by Roe *et al.*[1] and others[2] of a sensory deficit in the anal canal using the technique of mucosal electrosensitivity.

They suggest that, because the minimal detectable temperature change (MDTC) in the anal canal is small in normals and significantly higher in IFI, temperature sensation is important in normality and may be contributory in incontinence.

Consider the situation of a hot object (temp. θ_2°C) placed against the skin (temp. θ_1°C). The change of temperature of the skin/object interface with time is illustrated in *Figure 1* for: an object of high thermal conductivity; low thermal conductivity; and for an object of high thermal conductivity and infinite thermal capacity. If a substance of low thermal conductivity is used then the rate of change of temperature at the interface may be insufficient to exceed the rate of adaptation of the temperature receptors and either fail to produce a conscious appreciation of temperature change or delay its appreciation until a higher threshold has been reached.

The MDTC is small because of the high thermal conductivity of the brass tip and infinite thermal capacity of the system, by virtue of the constant perfusion of water maintained at constant temperature.

They suggest that discrimination of gas, liquid and solid may be dependent on normal temperature sensation due to an appreciation of the thermal mass of the substance palpated. This, and their analogy to differentiating between a metal and plastic object at the same temperature, is suspect. Thermal mass or thermal capacity is the product of the mass (M, in kg) of the object and its specific heat capacity (S, in J kg^{-1} °C^{-1}), expressed as MS J °C^{-1}. A plastic object could have the same thermal capacity as a metal object (by increasing its mass), be at the same temperature and still feel different because of its thermal conductivity. It is the difference in thermal conductivity that allows the discrimination between the two objects at the same temperature and not thermal capacity.

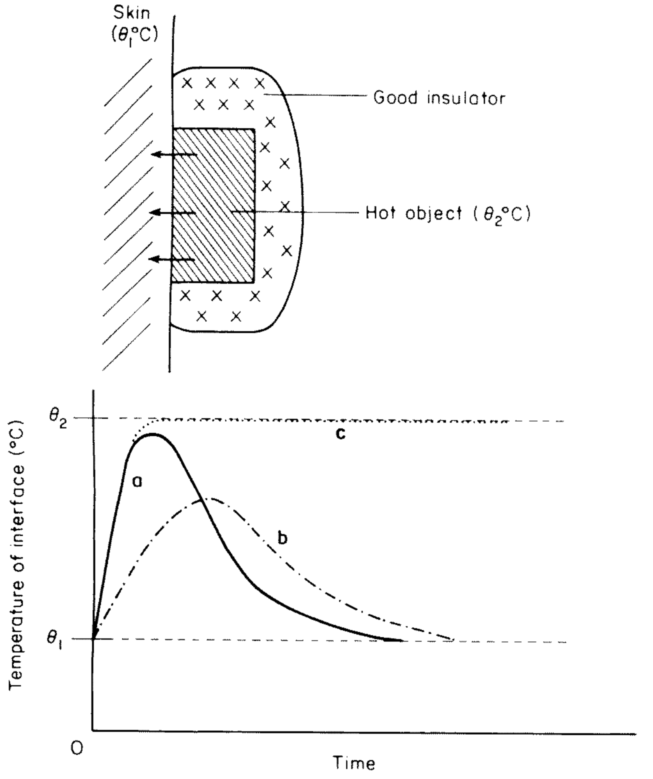

Figure 1 *The change of temperature at the skin/object interface with time in an object of* **a**, *high thermal conductivity;* **b**, *low thermal conductivity; and* **c**, *high thermal conductivity and infinite thermal capacity*

Furthermore, to appreciate a difference in temperature requires a temperature gradient, in this case between the object and the skin. In other words an object in thermal equilibrium with the skin will not stimulate the temperature receptors as it will neither give up heat nor extract heat. Thus to suggest that temperature sensation is important in the anal canal it would have to be shown that a temperature gradient exists between the rectum and anal canal or, better still, the faecal residue and anal canal. The authors have shown no data to support the existence of a gradient. Even if a gradient did exist it would have to be of sufficient magnitude to generate the minimal detectable temperature change at a rate equivalent to that generated by the probe used in this experiment. It is unlikely that faecal material has anything like the thermal conductivity of brass or the near infinite heat capacity of the water perfused system used.

The authors have shown that temperature sensibility exists in the anal canal in normals and that it is deficient in patients with IFI. Their data do not support speculation that temperature sensation is important in discrimination of gas, liquid or solid, or that decreased temperature sensibility is in anyway contributory to the pathogenesis of faecal incontinence.

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1. Roe AM, Bartolo DCC, Mortensen NJMcC. New method for assessment of anal sensation in various anorectal disorders. *Br J Surg* 1986; **25**: 1279–82.
2. Rogers J, Misiewicz JJ, Henry MM. Combined sensory and motor deficit in primary neuropathic faecal incontinence. *Gut* 1987; in press.

Authors' reply

Sir

We are grateful for the opportunity to reply to Mr Rogers' letter. His suggestion that the low thermal thresholds in normal patients are due to the high conductivity of our thermode reveals a misunderstanding of our technique. Thermal conductivity affects sensory thresholds by altering the rate of temperature change of the skin/thermode interface, poorly conducting materials feeling warmer as they produce a slower rate of temperature change than those having good conduction.

Sensory thresholds are commonly assessed by imposing changes in the adequate stimulus of the sensory receptor under study. It is well known that cutaneous thermoreceptors respond best to thermal change and poorly to steady temperature. It is clearly necessary, therefore, that any device used to assess thermal threshold must be of high thermal conductivity to be able to conduct heat to, or from, these receptors. The actual rate of change of temperature can then be modified as the investigator wishes, in our case by varying the flow rate and temperature of the water perfusing through the thermode. This is a well documented technique frequently used in sensory physiology[1].

The presence of a thermal gradient along the anorectum is indeed an important element of our hypothesis as rightly pointed out by Mr Rogers. We have investigated this in a study of 21 patients and have found significant temperature differences between the rectum and mid-anal canal (median, 0·3°C; range, 0–0·6°C) and rectum and lower anal canal (median, 0·5°C; range, 0·2–0·7°C). Since the anal canal is so exquisitely sensitive we suggest that it would be able to appreciate these temperature differences.

Our more recent work on the role of sensation in the continence mechanism has demonstrated that in health there are frequent repeated sampling episodes during which rectal contents could come into contact with this highly sensitive anal mucosa. This activity is impaired in incontinent patients[2]. Our suggestion about the role of temperature sensation in continence is a working hypothesis. There is a growing body of evidence in support of this proposal.

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1. Fruhstorfer H, Detering I. A simple thermode for rapid temperature changes. *Pflügers Arch* 1974; **349**: 83–5.
2. Miller R, Bartolo DCC, Cervero F, Mortensen NJMcC. Anorectal sampling: a comparison of normal and incontinent patients. *Br J Surg* 1988 (in press).

Postoperative gastrointestinal atony

Sir

It is a pity that Dr M. Verlinden and his colleagues (*Br J Surg* 1987; **74**: 614–17) have not studied the usual pattern of return of gut motility after abdominal surgery, as they would then have not made a series of errors.

Firstly, the motility of the entire gastrointestinal tract is not inhibited after operation—the small intestine continues to exhibit the passage of the interdigestive motor complexes (IDMC) after surgery. Motility of the colon may be reduced but is not absent.

Secondly, recurrence of function does not occur from stomach to the rectosigmoid, but rather small intestine, colon and stomach last. This has been clearly demonstrated by barium studies after such surgery as partial gastrectomy and truncal vagotomy. It has been demonstrated many times that fluids, e.g. glucose drinks, absorbable contrast agents, introduced into the small intestine within 24 h of such surgery are promptly absorbed[1,2].

The absence of bowel sounds after abdominal surgery has been equated with total loss of motility of the gastrointestinal tract. This is fallacious. The small intestine rapidly empties itself of contents as a result of the IDMC (the 'housekeeper phenomenon'). Thereafter, contractions without gas are silent. Return of bowel sounds indicates that the stomach has resumed contraction and is once more passing gas into the active small intestine which is responsible for most noise.

Finally, if, as the authors state, the gut in inhibited why do they propose stimulatory drug therapy? Would not release of the inhibition—whatever that might be—be more appropriate?

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1. Rothnie NG, Kemp Harper RA, Catchpole BN. Early postoperative gastrointestinal activity. *Lancet* 1963; **ii**: 64–7.
2. Wells C, Rawlinson K, Tinckler L, Jones H, Saunders J. Ileus and postoperative intestinal motility. *Lancet* 1961; **ii**: 136–7.

Correct placement of a permanent endo-oesophageal tube

Sir

Auscultation in the epigastrium as a means of determining correct placement of an endo-oesophageal tube (*Br J Surg* 1987; **74**: 419) has previously been described[1]. However, this method does not reliably differentiate between correct placement of the tube and abdominal oesophageal perforation. A more reliable method, in the absence of fibre-optic endoscopy, is to pass a nasogastric tube through the endo-oesophageal tube and aspirate acid on litmus paper, thus confirming free passage into the stomach.

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1. Watters DAK. The surgical treatment of oesophageal cancer. *Proc Assoc Surg E Afr* 1985; **8**: 99–106.

Salvage autotransfusion in aortic surgery

Sir

I wish to congratulate Mr P. C. Clifford *et al.* for their article (*Br J Surg* 1987; **74**: 755–7) which like mine[1] serves to re-awaken interest in autologous blood transfusion. The advantages of intra-operative autologous blood transfusion are enormous. Reduced dependence on homologous bank blood is essential at the present time in view of the risk of transmission of AIDS. The frequency and importance of such complications as consumption coagulopathy, dilutional coagulopathy, pulmonary insufficiency due to micro-emboli, fatal air embolism, hepatic failure and renal failure have hitherto been over-stressed. Major complications are not usually encountered when less than 3000 ml of autologous spilt blood are retransfused to the patient. Antibiotics which can be used perioperatively effectively reduce the risk of sepsis which should not contra-indicate autologous blood transfusion in emergency situations where homologous bank blood is not immediately available[1]. The Cell saver and cell washing machines also make autologous blood transfusion possible even in the presence of frank sepsis or malignancy. The solcotrans disposable device reduced the operation time in my series but the cost may prohibit its use by doctors working in the developing countries.

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1. Efem SEE. Noninvasive technique of intraoperative autologous blood transfusion in abdominal vascular accidents. *Vasc Surg* 1987; **21**: 1–3.

Surgical technique

Sir

Your leading article on surgical technique raises important implications for British surgery (*Br J Surg* 1987; **74**: 763–4). The practice of surgery is largely a craft and we know innately that the quality of craftsmanship influences outcome. As surgeons we have always acknowledged it and take full account of it, along with other qualities such as compassion and judgement, when choosing a colleague to treat ourselves and our families. The public remain naive and in general have unquestioning faith that all surgeons must inherently be masters of their craft. As a profession we have in recent years let them down.

In the distant past a surgeon was judged by, and his reputation based on, technical prowess. During the past 30 years or so surgery has veered in a scientific direction and reputations are now largely based on scientific contribution. Perhaps more so in Scotland than in the UK as a whole, academic surgery holds the reins of influence. Concurrently, the attitude that operative surgery is easy, routine, universally adequate and not a sufficient intellectual stimulus for intelligent men has been tacitly promoted. A well known statement to that effect coupled with the view that surgeons ought to direct their energies to physiological research is attributed to one of the father figures of Scottish academic surgery.

Academic appointments are made largely on the basis of original scientific contribution and potential and seldom is any consideration given to craftsmanship. I do not argue with that but unless the head of an academic department is at least the equal of his consultant colleagues in craftsmanship the potential for even local leadership is low. Although there are notable exceptions, those who concentrate in their formative years on research and spend much of their time later on travel are inherently unlikely, unless inordinately gifted, to maintain and to improve their technical ability and are also unlikely to acknowledge its fundamental importance.

At the same time considerations other than clinical and technical ability dominate NHS consultant appointments. As a member of Advisory Appointments Committees in the role of National Panelist and otherwise, I have seldom heard technical skill aired as an important criterion of appointment. Scientific contribution and potential however usually weigh heavily, though many are realistically ready to shed their scientific mantle on appointment. Every trainee, however limited his aptitude, is expected to have undertaken research, published several papers and written a high degree. I do not imply that these pursuits do not augment the trainee's ultimate clinical performance but would a year spent in travel to centres of clinical excellence (as was the custom long ago) profit many a trainee more than a year devoted to an often esoteric and paraclinical research project?

It is a welcome trend that differences in craftsmanship are now being written about and openly recognized as crucial to surgical outcome. That recognition is the foundation for re-assertion of the importance of technical skill as a necessary attribute for a surgical career. I do not think that technical skill can ever be subject to structured examination and do not believe it necessary to attempt it. Examinations for fellowship of the surgical colleges are simply tests of assimilation of knowledge, minor hurdles along the way of surgical training. Technical ability however should be a major consideration in the regular local review of trainees on a rotational programme and those who are inadequate technically should be counselled at an early stage and led in other directions. In addition, if we are now ready to admit that surgery as a craft is a worthy challenge and not almost to be despised intellectually (it has always been difficult enough and sufficiently challenging for me) we should make sure that technical ability and performance are prime considerations when making NHS consultant appointments.

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Book reviews

Wound Care

W. M. Cocke. 182 × 269 mm. Pp. 120. Illustrated. 1986. Edinburgh: Churchill Livingstone. £21.00.

According to the authors, four plastic surgeons from Texas, this book is a practical guide to wound care intended for surgeons, physicians, nurses, and physical therapists. The text refers to the care of skin wounds and begins with a brief account of the basic principles of repair and the factors which may affect wound healing. Strangely, the same subject is repeated in the next chapter. Subsequent sections deal with the techniques of care in abrasions, lacerations, burns, ulcers, bite wounds, and 'difficult' wounds including those of the lower extremities, blast injuries, and irradiated tissue.

The style is dogmatic and there are no references to published work. However, some of the recommendations are controversial, unsubstantiated, or ill-defined: the authors eschew the recent innovations in wound dressings; the antibiotics used in topical or systemic prophylaxis are unspecified; and the adverse effects of trace metal deficiency and the value of hyperbaric oxygen therapy in wound healing are exaggerated.

I found the book rather disappointing. The SHO commencing his surgical career or the assistant in the accident and emergency department might benefit by reading the section on the care of simple skin wounds and techniques of skin closure, but the vast majority of the more serious wounds described in this book rightly belong to plastic surgeons in the UK, and the book is of interest rather than practical value to the general surgeon.

T. T. Irvin

Progress in Transplantation. Volume 3

P. J. Morris and N. L. Tilney. 160 × 240 mm. Pp. 217. Illustrated. 1987. Edinburgh: Churchill Livingstone. £40.00.

This little book of some 200 pages has been edited by two respected transplant surgeons, one from each side of the Atlantic. They have undertaken the very formidable task of trying to document progress in a subject which is evolving so fast that new discoveries tend to be overtaken very quickly. To help them in their task they have recruited a number of clinicians and immunologists in the forefront of transplantation research, and the book itself is a nice blend of topics selected from some areas of progress in clinical and immunological aspects of transplantation.

It is a book which is easy to read and can be understood by those with a general knowledge of transplantation biology. As one would anticipate in any book, there are a number of minor criticisms that can be made which often reflect a different viewpoint by the reviewer. For example, in the chapter on chemical suppression of the immune response one would wonder at the need to discuss cyclophosphamide and niridazole which are hardly ever used but, even more, one would question the statement that says corticosteroids are 'almost mandatory' in immunesuppression when much of the benefit of modern immunesuppression has been to allow the minimization and even omission of corticosteroids from the modern treatment regimes.

Generally, the book achieves what it sets out to do and brings together up-to-date information in the chosen areas of transplantation. The reference list is extensive and the book will satisfy those who wish a quick revision and explanation of the current status of some aspects of transplantation. It will not satisfy the scientist and researcher who will still go to the journals to remain completely at the forefront of his chosen area.

R. Taylor

Case Presentations in General Surgery

T. V. Taylor. 130 × 210 mm. Pp. 205. 1987. London: Butterworths. £8.95.

Each of the 64 cases has been presented with a concise history, initial list of investigations and a range of questions which differ from case to case. This is followed by a discussion covering differential diagnosis and management. Although providing a revision test, the main purpose of this book must be in helping candidates prepare a case for presentation. Generally an extremely well written book, up-to-date and not too controversial. The authors aimed this book at the final MB and the final FRCS, and probably by its nature it is applicable to both groups of candidates, but its main value lies in demonstrating the correct presentation of a case.

J. Scurr

Trauma. Emergency Surgery and Critical Care

J. H. Siegel. 185 × 260 mm. Pp. 1206. Illustrated. 1987. Edinburgh: Churchill Livingstone. £130.00.

This volume is edited by Dr Siegal who is Deputy Director of the Maryland Institute for Emergency Medical Services System. This organization is responsible for the co-ordination of trauma and emergency services in the State of Maryland which has a population of 4·3 million, and clearly provides an abundance of clinical material.

The Editor, in his preface, states that the trauma surgeon is the captain of a team, and he has amassed a large number of contributing specialists ranging from thoracic surgeons to psychiatrists. Half the contributors are colleagues of Dr Siegel's from Baltimore who testify to the co-ordinated multidisciplinary approach.

There are large detailed sections dealing with hypovolaemic shock, cardiogenic shock, septic shock and the adult respiratory distress syndrome. The problems are illustrated by discussing difficult clinical cases, such as a young man with post-traumatic myocardial contusion who was suffering from low output syndrome from a liver laceration and was successfully managed with an intra-aortic counter pulsation balloon.

I found the discussion on the accuracy of peritoneal lavage as a diagnostic tool particularly helpful, as I did the section on post-traumatic coagulation defects. Their protocols for the management of a severely injured patient indicating orders of priority are complex, but clearly very well worked out. The emphasis in this book is on the intensive care aspect of the shocked trauma patient and less space is given to the operative management of, for instance, liver injuries, splenic repair, and bullet injuries; I found this disappointing. This book is for those with a major commitment to intensive care medicine, and particularly to the trauma patient, in the ICU. The book costs £135.00 and I think is unlikely to be bought by most general surgeons. I would, however, like it to be in the hospital library for ready access.

W. J. Owen

General Surgical Operations. Second edition

R. M. Kirk and R. M. C. Williamson. 223 × 282 mm. Pp. 649. Illustrated. 1987. Edinburgh: Churchill Livingstone. £48.00.

Only 7 of the original 19 contributors are retained in the second edition of *General Surgical Operations*. The present 25 authors have rewritten many of the chapters, but the original format has been retained. The standardized layout is for ease of reference, but I found the rigid adherence to the following alliterations rather irksome: appraise, assess, access, action and aftercare. The difference between appraise and assess is not always obvious and access is, surely, only part of action. By sticking to this layout there is often unnecessary repetition, as in chapter 5 where we are told on no less than 12 occasions to make an upper midline or paramedian incision for access. Surgery is controversial and there are many points with which all surgeons would not agree. For example: palpation of the whole of the small bowel routinely at all laparotomies (page 47); 5 cm clearance for cancer of the rectum (page 130); excision of 5–10 cm of normal small bowel beyond the lesion in Crohn's disease (page 131); nasogastric intubation for 12–24 h after cholecystectomy (page 174); and suture closure of an evacuated perianal haematoma (page 156).

The book is aimed at surgeons in training and is excellent for candidates for the FRCS examination. Its wide cover includes plastic surgery, neurosurgery, gynaecology, ophthalmology, otolaryngology, oral surgery, orthopaedics and trauma in sufficient depth for the examination. Because of its comprehensive nature, it cannot give the necessary operative detail for the trained surgeon who merely wants to remind himself of some of the finer points of an operation. The book is well illustrated with over 700 line drawings, and is reasonably priced at £48.00.

G. W. Johnson

Notices and announcements

19–21 December 1987
2nd International Surgical Congress and Workshop on 'Surgical Manpower and Technology—Development and Utilization in Developing Countries'
Dhaka, Bangladesh
Information: Professor Golam Rasul, Department of Surgery, Institute of Post-Graduate Medicine and Research, Shahbag, Dhaka, Bangladesh.

23–24 January 1988
Hong Kong Surgical Forum Winter 1988
Hong Kong
Information: Forum Secretary, Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong

28–29 January 1988
International Colloquium on Cardiac Reconstructions
Salzburg, Austria
Information: American Express, Mr Blümel, Mozartplatz 2, A-5020 Salzburg, Austria

4–9 February 1988
54th Annual Meeting of the American Academy of Orthopaedic Surgeons
Atlanta, USA
Information: Lois Stratmeier, 444 North Michigan Avenue, Suite 1500, Chicago, Illinois 60611-3981, USA

8–12 February 1988
Third Biennial Conference of the Indian Society of Oncology and the Indo–USSR International Workshop on Oesophageal Cancer
Bangalore, India
Information: Conference Secretariat: Kidwai Memorial Institute of Oncology, Hosur Road, Bangalore-560 029-India

3–5 March 1988
1st International Congress on the Immune Consequences of Trauma Shock and Sepsis, Mechanisms and Therapeutic approaches
Munich, FRG
Information: Dr Eugen Faist, LM University Munich, Department of Surgery, Klinikum Grobhadern, Postfach 701260, D-8000 Munich 70, FRG

13–15 April 1988
Annual Meeting of the Association of Surgeons of Great Britain and Ireland
Harrogate, UK
Information: Mr B. T. Jackson., The Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London WC2A 3PN, UK

17–28 April 1988
Advances in Neurosurgery
Glasgow/Edinburgh, Scotland, UK
Information: Director, Courses Department, The British Council, 65 Davies Street, London W1Y 2AA, UK

21–23 April 1988
2nd Symposium for Surgery on the Fetus
Gmunden, Germany
Information: Dr Wolfgang Metka, A-4020 Linz, Hauptplatz 29, Germany

1–6 May 1988
Bicentennial Scientific Meeting Royal Australasian College of Surgeons
Brisbane, Australia
Information: 1988 GSM, Royal Australasian College of Surgeons, Spring Street, Melbourne, Australia 3000

5–7 May 1988
Biennial Congress of the European Council of Coloproctology 1988
Geneva, Switzerland
Information: General Secretary of the European Council of Coloproctology, Policlinique de Chirurgie, Hôpital Cantonal Universitaire de Genève, 1211 Geneva 4, Switzerland

8–11 May 1988
Joint Annual Meeting of the American Lung Association, the American Thoracic Society and the Congress of Lung Association Staff
Las Vegas, USA
Information: Deborah Richardt, American Lung Association, 1740 Broadway, New York 10019, USA

12–14 May 1988
Second Vienna Shock Forum
Vienna, Austria
Information: AUSTROPA Kongbressbüro, Friedrichstrasse 7, A-1010 Vienna, Austria

22–28 May 1988
VII Iberolatinamerican Congress of Plastic Surgery
Cartagena, Colombia
Information: Sociedad Colombiana De Cirugia Plástica, Ap. Aéreo Nos 6658; 6572, Bogota DE, Colombia, South America

25–28 May 1988
79th Annual Meeting of the American Association for Cancer Research
New Orleans, Louisiana, USA
Information: Margaret Foti, Executive Director, American Association for Cancer Research, Temple University School of Medidine, West Building Room 301, Philadelphia, PA 19140, USA

29 May–3 June 1988
Second World Congress on Hepato-Pancreato-Biliary Surgery
Amsterdam, The Netherlands
Information: Q. A. Laman Trip, Organizer, Alton House, Keizersgracht 792, 1017 EC Amsterdam, The Netherlands

5–11 June 1988
Tropical Medicine Update
Liverpool, UK
Information: Director, Courses Department, The British Council, 65 Davies Street, London W1Y 2AA, UK

12–17 June 1988
Cardiovascular and Interventional Radiological Society of Europe
Berlin, FRG
Information: Dr Reingard Sörensen, Klinikum Steglitz, Röntgendiagnostik, Hindenburgdamm 30, 1000 Berin 45, FRG

20–22 June 1988
7th International Workshop for the Study of Vascular Anomalies
Hamburg, Germany
Information: Dr John B. Mulliken, The Children's Hospital, 300 Longwood Avenue, Boston MA 02115, USA

29 June–1 July 1988
International Symposium on Therapeutic Progress in Urological Cancers
Paris, France
Information: Dr Saad Khoury, Clinique Urologique (Pr Chatelain), Hôpital de la Pitié, 83 Bd de l'Hôpital, 75634 Paris, Cedex 13, France

3–9 July 1988
16th World Congress of the International College of Surgeons
Milan, Italy
Information: Secretariat, Clinica Chirurgica III—Università degli Studi, Via F Sforza 35, 20122 Milan, Italy

6–8 July 1988
The Third British Arthroscopy Symposium
Harrogate, UK
Information: Mr M. R. Phillips, Chas F. Thackray Ltd., Shire Oak Street, Leeds LS6 2DP, UK

9–10 July 1988
Hong Kong Surgical Forum Summer 1988
Hong Kong
Information: Forum Secretary, Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong

30 August–2 September 1988
10th World Congress Collegium Internationale Chirurgiae Digestive
Copenhagen, Denmark
Information: Secretariat, Spadille Congress Service, Sommervej 3, DK-3100 Hornbaek, Denmark

11–19 September 1988
XIIth International Congress of the Transplantation Society of Australia and New Zealand
Sydney, Australia
Information: Dr B. Hall, Honorary Secretary, Transplantation Society of Australia and New Zealand, 145 Macquaire St, Sydney 2000, Australia

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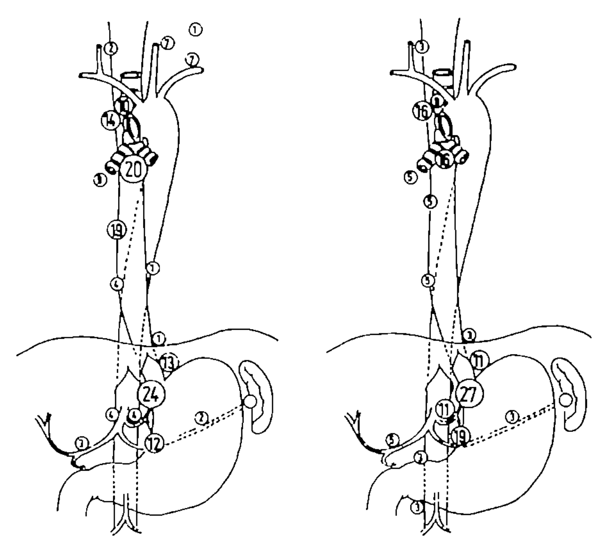

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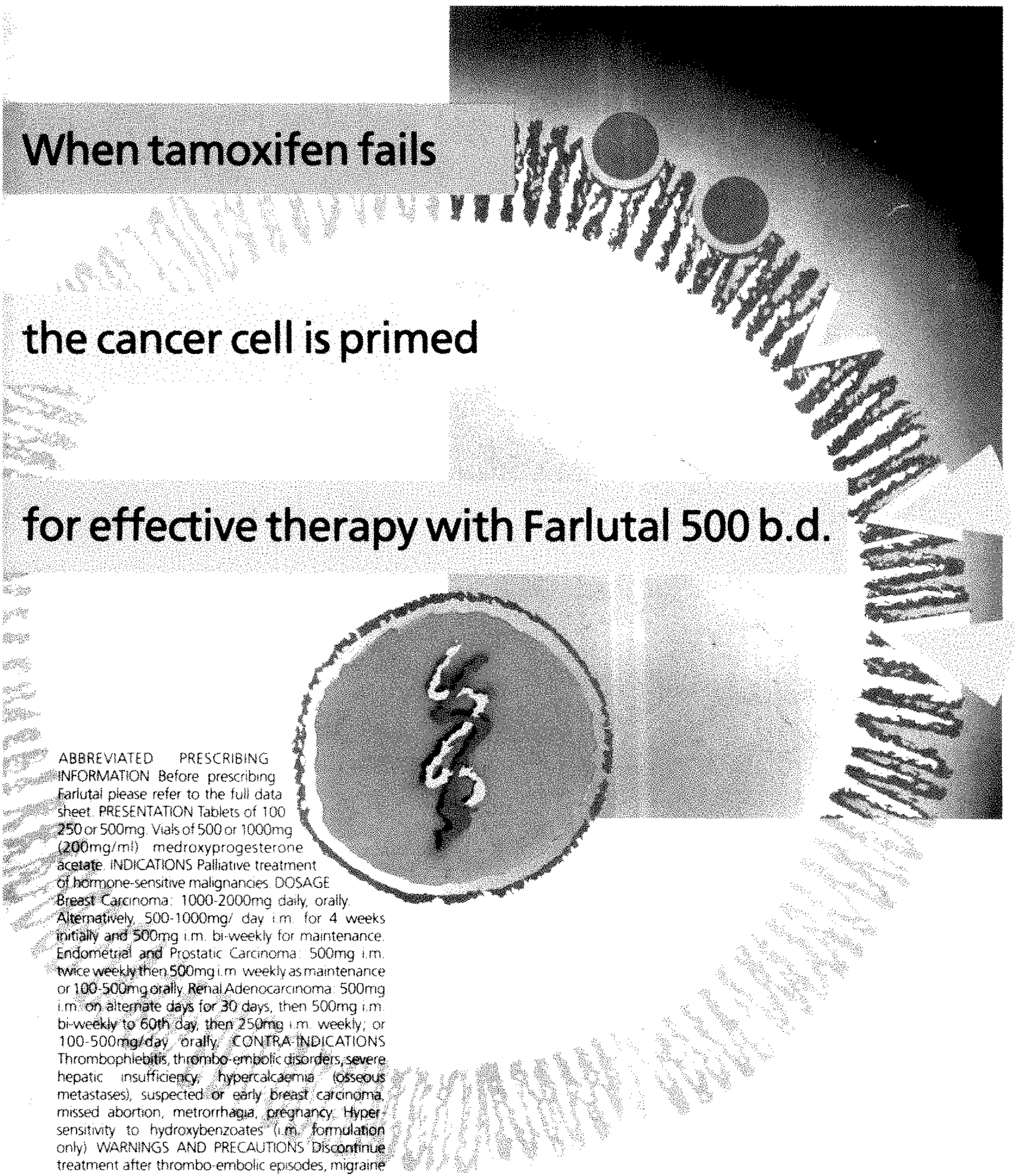

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